

^{133}Xe -RADIOSPIROMETRY

A clinical method for studying regional lung function

BY

GUNNAR MIÖRNER

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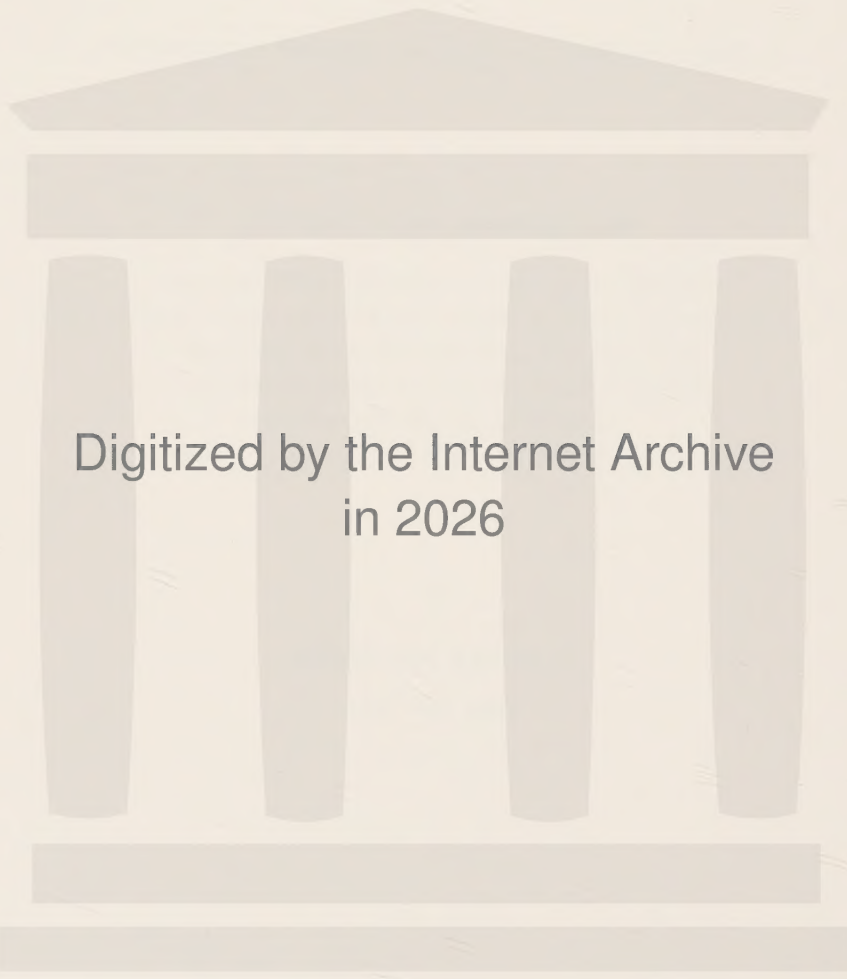
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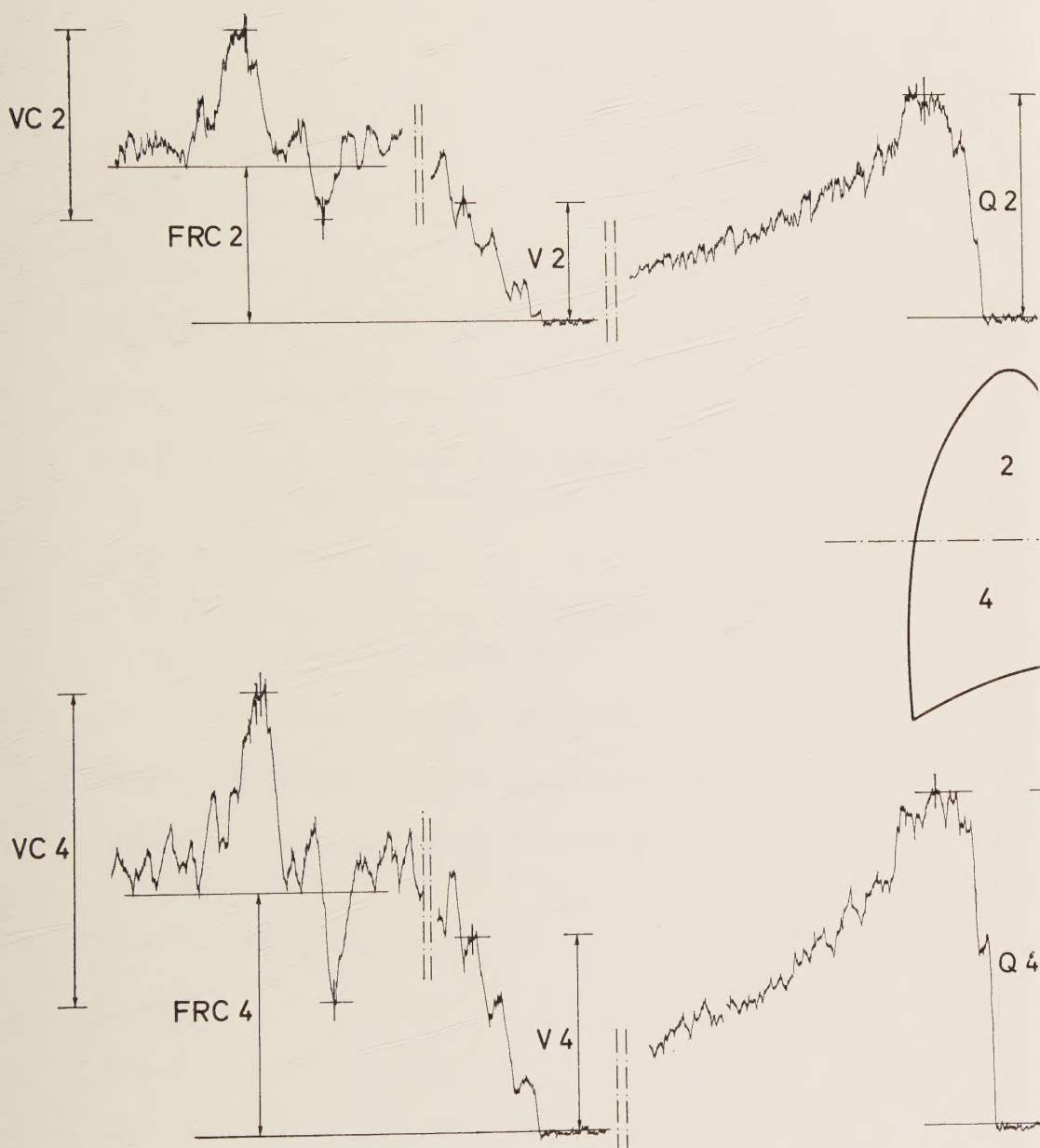
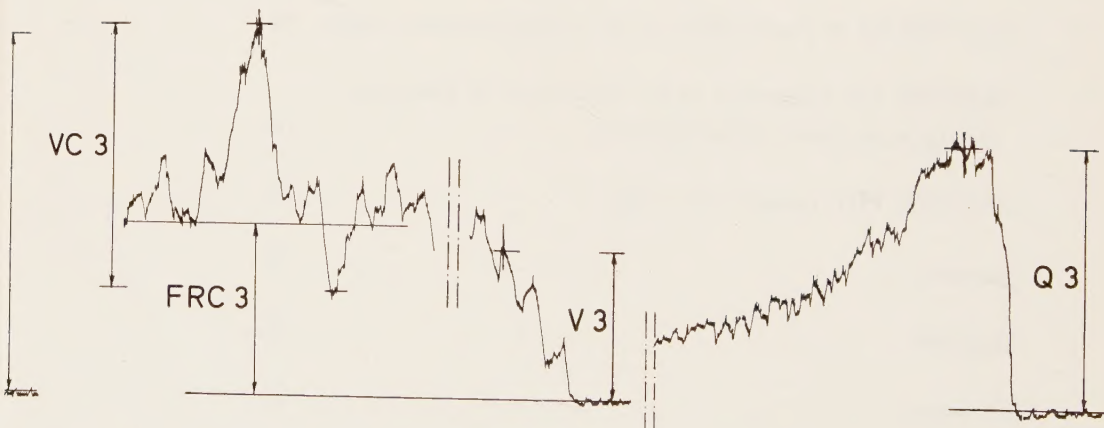
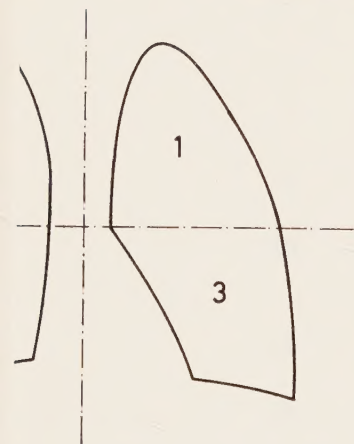
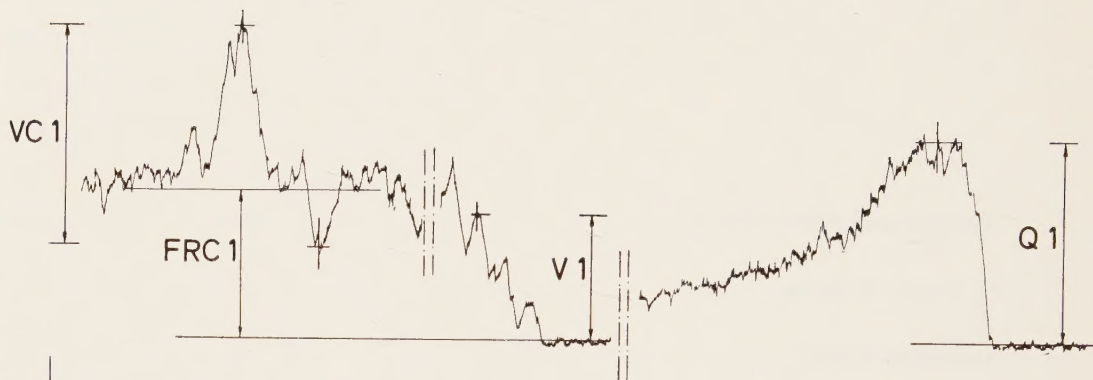


Fig. 1. Records from a normal subject in



relation to the four recording channels.

SYMBOLS AND ABBREVIATIONS

Xe-133	¹³³ Xenon
Q	Perfusion
V	Ventilation
FRC	Functional residual capacity
VC	Vital capacity
MVV	Maximal voluntary ventilation
FEV _{1.0}	Forced expiratory volume in one second
Q 1 — Q 4	See Fig. 1! Q 1 stands for the regional perfusion of the upper half of the left lung, estimated as shown in the figure, <i>i.e.</i> as the counting rate recorded from this lung field after an intravenous injection of Xe-133. Similarly Q 2, Q 3 and Q 4 are used as estimates of the regional perfusion of the other three lung fields.
V 1 — V 4	In the same way V 1 stands for the estimate of the regional ventilation of the upper half of the left lung as indicated in Figure 1. V 1 is measured after the three first breaths from a spirometer containing Xe-133.
FRC 1 — FRC 4	FRC 1 is used as an estimate of the lung volume (at end-expiratory level) in the upper half of the left lung. It is recorded at the end of the re-breathing period.
VC 1 — VC 4	VC 1 is the difference in the counting rate of the same lung field between a maximal inspiration and a maximal expiration at the end of the re-breathing period. In all these measurements corrections have been made for any differences in sensitivity between the four recording channels.
Q I — Q IV	The counting rates recorded from fields 1—4 expressed as <i>per cent</i> of the sum of the counting rates in all four fields, <i>e.g.</i> $Q I = \frac{Q 1}{Q 1 + Q 2 + Q 3 + Q 4} \times 100 \quad \text{etc.}$
V I — V IV	are similarly defined, <i>e.g.</i> $V C I = \frac{V C 1}{V C 1 + V C 2 + V C 3 + V C 4} \times 100$
FRC I — FRC IV	
VC I — VC IV	

$Q R$
 $Q L$
 $V R$
 $V L$
 $FRC R$
 $FRC L$
 $VC R$
 $VC L$

The counting rates recorded from the right and left lung, respectively, expressed as *per cent* of the sum of the counting rates in all four fields, *e.g.*
 $Q R = Q II + Q IV$
 $Q L = Q I + Q III$ etc.

$Q Ra$
 $V Ra$
 $FRC Ra$
 $VC Ra$

The counting rates recorded from the right apical field (2) in *per cent* of the sum of the counting rates recorded from *both* apical fields (1 and 2), *e.g.*
 $Q Ra = \frac{Q 2}{Q 1 + Q 2} \times 100$ etc.

$Q Rb$
 $V Rb$
 $FRC Rb$
 $VC Rb$

The counting rate recorded from the right basal field (4) in *per cent* of the sum of the counting rates recorded from both basal fields (3 and 4), *e.g.*
 $Q Rb = \frac{Q 4}{Q 3 + Q 4} \times 100$ etc.

La and Lb are used in analogy with Ra and Rb .

ind. $Q I$ — ind. $Q IV$ The perfusion index for lung fields 1—4, *e.g.*
 ind. $Q I = \frac{Q I}{FRC I}$ etc.

ind. $V I$ — ind. $V IV$ The ventilation index for lung fields 1—4, *e.g.*
 ind. $V I = \frac{V I}{FRC I}$ etc.

$V/Q I$ — $V/Q IV$ Ventilation/perfusion ratio for lung fields 1—4, *e.g.*
 $V/Q I = \frac{V I}{Q I}$ etc.

STATISTICAL METHODS

$$\text{Arithmetic mean} = m = \frac{\sum x}{n}$$

$\sum x$ = sum of all observations x = individual observation n = number of observations

Mean difference = arithmetic mean of the differences

The error of a single observation was determined from the difference between paired observations (d) according to the formula:

$$e = \sqrt{\frac{\sum d^2}{2n}}$$

Standard deviation (SD) was calculated according to the formula: $SD = \sqrt{\frac{\sum (x-m)^2}{n-1}}$

Normal-probability Paper and tolerance intervals: see Dixon and Massey (1957).

F-test, linear regression and analysis of variance: see Mood and Graybill (1963).

INTRODUCTION

The importance of spirometry in the preoperative evaluation of patients for pulmonary surgery is well established (Birath 1954; Bates & Comroe 1966).

It seems a priori that methods which allow evaluation of the function of each lung separately would be of great value in pulmonary surgery. For this purpose bronchspirometry was introduced as early as 1934 by Björkman and further developed by Carlens (1949). The usefulness of bronchspirometry as a research instrument has been well documented in the studies by Pinner, Leiner and Zavod (1945), Gaensler and Watson (1952), Inada, Kishimoto, Sato and Watanabe (1954), Svanberg (1957), Arborelius, Ekvall, Jernérus, Lundin and Svanberg (1962) and Arborelius (1966). Bronchspirometry has, however, become routine method only in very few laboratories, probably because it requires extensive training for the investigator if discomfort in connection with the investigation is to be avoided. A method which permitted the evaluation of the function within each lung separately, and perhaps also within different regions of each lung, would be of great clinical value if it were as simple and non-injurious as spirometry.

Radioactive gases such as Xe-133, $^{15}\text{O}_2$, C^{15}O_2 and C^{15}O have been used in the investigation of regional lung function (Knipping, Bolt, Venrath, Valentin, Ludes & Endler 1955; Dyson, Hugh-Jones, Newbery & Sinclair 1960; West & Dollery 1960; Dollery, Dyson & Sinclair 1960; Ball, Stewart, Newsham & Bates 1962; Dollery, Hugh-Jones & Matthews 1962; Anthonisen, Dolovich & Bates 1966). The techniques published differ widely and no serious attempt has been made to validate the methods used to measure regional ventilation, perfusion and volume with the aid of bronchspirometry.

The purpose of the present investigation has been to develop a technique for studying regional lung function which would be simple enough to use in clinical routine and yet render information comparable to that obtained with bronchspirometry. The technique which will be presented here uses Xe-133 and is henceforth called radiospirometry.

Chapter I is a brief review of literature covering bronchspirometry and radio-nuclids in the study of regional lung function. Various factors of importance in the choice of technique are discussed in Chapter II. Chapter III contains a description of the technical equipment and the procedure for a routine radiospirometry.

Chapter IV contains a comparison between radiospirometry and bronchosprometry in 35 patients with pulmonary diseases. In view of the promising results from this comparison it was decided to study the most useful parameters in the radio-spirogram further.

Chapter V presents the radiospirometric data from healthy volunteers.

The reproducibility of the different parameters used is further studied in Chapter VI. The results of the evaluation of regional perfusion during maintained breathing and during breath-holding are compared in Chapter VII.

Chapter VIII is a discussion of the findings in the present study in relation to other studies.

Chapter I

PREVIOUS INVESTIGATIONS

BRONCHOSPIROMETRY

The bronchspirometric technique has changed little since Carlens' double lumen catheter was introduced (1949).

The technique of bronchspirometry used in this laboratory was developed by Svanberg (1953 & 1957). Essentially the same technique was used by Arborelius (1966). Since the results of bronchspirometry were intended to serve as a frame of reference in judging the value of radiosprometry, it was desirable to know the methodological errors involved in bronchspirometry. Studies of the methodological error of bronchspirometry were first performed by Söderholm (1955), who made double determinations of ventilation, perfusion, and vital capacity at each examination in 75 patients with pulmonary disease. Svanberg (1957) studied the methodological error by repeating the bronchspirometric examination in healthy subjects on different days. Arborelius (1966) found a somewhat larger methodological error in patients with pulmonary disease than in healthy control-subjects. The results of these methodological studies in bronchspirometry are summarized in Table 1.

Table 1

Studies of the methodological errors in bronchspirometry.

Error of a single determination (right lung in per cent of total).

	Perfusion	Ventilation	FRC	VC	
Söderholm (1955)	3.8	3.5		1.7	75 pathological cases
Svanberg (1957)	1.9	3.3		1.8	9 normal subjects *)
			3.0		6 normal subjects *)
Arborelius (1966)	2.6	3.0			11 normal subjects
	4.1	3.2			25 pathological cases

*) 2 investigations on different days.

Both Svanberg (1957) and Arborelius (1966) reported figures for the distribution of perfusion, ventilation and lung volumes in healthy subjects (Table 2).

Table 2

Bronchspirometry in normal subjects (right lung in per cent of total).

Number of subjects		Position	Perfusion			Ventilation			FRC		VC	
			Mean	SD	Range	Mean	SD	Range	Mean	SD	Mean	SD
Svanberg (1957)	25	Supine	53	2.7	49-59	55	4.0	48-66			52	1.7
	25	Sitting	53	2.1	49-56	54	3.4	48-62			53	1.7
	20	Supine							55	3.6	48-63	
	14	Sitting							54	2.4	50-59	
Arborelius (1966)	24	Sitting	53.5	3.6	43.9-60.2	50.2	4.1	39.1-56.6			52.1	1.5
											48.7-55.3	

Bronchspirometry cannot localize a lesion within a lung. When the investigation is performed both in the sitting and the supine positions it can, however, sometimes help localize where in the lung the process which causes a reduction of perfusion is to be found (Svanberg 1955; Miörner & Svanberg 1963).

STUDIES OF REGIONAL LUNG FUNCTION WITH RADIONUCLIDS

In the beginning of the 1950's investigations of the regional distribution of ventilation with the aid of radionuclids were introduced at the University Clinic of Cologne (Knipping, Ludes, Valentin & Venrath 1953). The first substance used was ethyliodide labelled with ¹³¹I. However, this substance dissolved so easily in blood that the recordings were disturbed by the extra counting rate from the heart and the central blood vessels. Therefore it was soon decided to use Xe-133 instead and extensive studies of the distribution of ventilation in normal subjects were performed as well as in patients with pulmonary disease (Knipping et al. 1955; Valentin, Venrath & Markou 1956; Knipping, Bolt, Valentin, Venrath & Endler 1957; Knipping, Bolt, Valentin, Venrath & Endler 1958). Detailed regional studies were carried out using up to 16 Geiger-Müller tubes placed over the dorsal side of the thorax, but the value of these investigations is limited, as only the distribution of ventilation was studied. Several investigations of later date, beginning with Ball et al. (1962) at the Royal Victoria Hospital in Montreal, have shown that Xe-133 may be used for studies of regional ventilation as well as regional lung volume and regional perfusion. As at present Xe-133 seems to be the only suitable tracer which is generally available for

clinical use, the literature review will mainly deal with investigations using this isotope and especially with studies of methods which may be applied in clinical routine.

Studies of the regional lung function with $^{15}\text{O}_2$ were initiated at Hammersmith Hospital in London in the 1950's. The results of these investigations with $^{15}\text{O}_2$, C^{15}O_2 and C^{15}O have been reported in several papers. These investigations deal partly with regional perfusion, ventilation and diffusion in normal subjects (Dollery et al. 1960; Dollery, West, Wilcken & Hugh-Jones 1961 b; West 1962 a & b), and partly with studies in patients with heart or lung diseases (Dyson, Hugh-Jones, Newbery & West 1958; Dollery & West 1960; Dyson et al. 1960; West, Dollery & Hugh-Jones 1961; Dollery, West, Wilcken, Goodwin & Hugh-Jones 1961 a; Dollery et al. 1961 b). However $^{15}\text{O}_2$ is not generally available for clinical routine work, as its half-life is only two minutes and therefore a cyclotron is necessary in the immediate vicinity of the laboratory.

In addition to these gases, radionuclids in a non-gaseous state have been used, mostly in the form of ^{131}I labelled macroaggregates of human serum albumin in studies of the perfusion (Wagner, Sabiston, McAfee, Tow & Stern 1964; Lopez-Majano, Chernick, Wagner & Dutton 1964) and also, less commonly, in studies of the ventilation (Quinn & Head 1966). These investigations are rather easy to carry out. The standard equipment for scintigraphy can be used. The information obtained is restricted to an instantaneous photograph of the distribution of perfusion at the time of injection and of the distribution of ventilation at the time of inhalation, and the method does not permit studies of dynamic events such as the wash-in and wash-out of radioactive gas within different regions of the lungs. Nor can the distribution of perfusion and ventilation be related to the regional volume. For special purposes, such as early diagnosis of pulmonary emboli, this method seems nevertheless to be of practical importance (Sabiston & Wagner 1965).

In reviewing the literature on Xe-133 in studies of regional lung function, special attention was paid to the following details which were of interest in planning the present study:

- (1) Different ways to assess regional perfusion and ventilation.
- (2) The technical details (*e.g.* the arrangement of the counters, the level of pulse discrimination and the recording devices).
- (3) The presentation of the results.

The review of the literature about these details will be based on the original presentation of the technique using Xe-133 to study regional perfusion, ventilation and lung volume (Ball et al. 1962). This technique has been adopted in principle by several other authors and will be described.

Six stationary scintillation counters fitted with cylindrical lead collimators were directed towards the dorsal side of the chest. The discriminators were adjusted to accept impulses corresponding to an energy of 25 keV or more. The recordings were

made on a multi-channel tape-recorder from which each channel could be played back at desired speed and amplification.

The investigation included two steps: inhalation from a spirometer containing air with approximately 0.5 mCi Xe-133 per litre and intravenous injection of Xe-133 solution.

The subject was seated in a chair, breathing through a mouth-piece. Background counting rate was recorded when the subject was breathing room air. He was then connected to the closed spirometer circuit at the end of a normal expiration. He inhaled a normal tidal volume and held his breath, thereby reaching an "activity plateau" (I). Then he was instructed to inspire fully, hold his breath (plateau II) and after that to breathe normally again, still attached to the spirometer with xenon. When the wash-in was finished, *i.e.* when a stable concentration of Xe-133 in the spirometer circuit was reached, the same procedures were repeated and "activity plateau" III was obtained, representing the counting rate at the same lung volume as I, *i.e.* FRC + tidal volume, and plateau IV corresponding to the same lung volume as II, *i.e.* TLC. The concentration of xenon in the spirometer circuit was measured by a counter in the tubing leading to the patient. The functional residual capacity was determined by the helium dilution technique.

When most of the xenon had been washed out of the lungs, a known amount of Xe-133 (approximately 0.5—1.0 mCi) was injected into a cubital vein. The subject was instructed to take a slow, deep breath and to hold it at full inspiration. At this moment another plateau (V) was recorded at the same lung volume as plateaus II and IV. The concentration of xenon in the lungs was known at plateaus II and IV, *i.e.* it was assumed to be equal to the concentration recorded by the counter in the spirometer. As the counting fields of each counter were equal at I and III and at II and IV it was possible to calculate the intrapulmonary concentration at I and II from the external counting rates. These concentrations were compared to the concentration which would be reached in all parts of the lung, if the distribution were uniform as estimated from the lung volume (FRC + tidal volume and TLC, respectively), the volume inhaled from the spirometer and the concentration of xenon in the spirometer. Thus distribution indices were calculated, expressing the total amount of xenon per unit volume delivered to the counting field as a percentage of the total amount per unit volume delivered to the lung as a whole. If the distribution were entirely uniform, the indices would be 100. The concentration of xenon at plateau V was calculated from the external counting rates at V and IV. The "ideal" concentration was estimated from the amount of xenon injected and from TLC. Distribution index for perfusion was calculated similarly to the distribution index for ventilation.

Since the indices were calculated from the ratio of two external counting rates, they were not dependent on counter sensitivity, volume of lung "seen" by the counter or of absorption of radiation by the chest wall.

(1) *Different ways to assess regional perfusion and ventilation.*

In Ball's study (Ball et al. 1962) *perfusion* was determined during breath-holding at maximal inspiration. The authors suggest that the distribution of perfusion might be different at maximal inspiration and at normal breathing. Miörner (1967a) measured counting rate during breath-holding at the end of a normal expiration and Heckscher, Larsen and Lassen (1966) when the subject was breathing normally. Ball et al. (1962) expressed the distribution of *ventilation* as static indices based on the distribution during breath-holding after a tidal breath and after a maximal inspiration. As pointed out in a later paper from the same group, this method has certain limitations (Bentivoglio, Beerel, Bryan, Stewart, Rose & Bates 1963a). After the inhalation of a tidal breath the counting rate is often low and consequently the random error is rather large in proportion to the counting rate, which makes it difficult to detect minor ventilatory abnormalities. Furthermore, the distribution of a single maximal breath is an incomplete description of the dynamic distribution of ventilation during normal breathing. Under these conditions the distribution is primarily determined by the regional compliance, as the airway resistance influences the distribution very little. In another study, Bentivoglio, Beerel, Stewart, Bryan, Ball and Bates (1963b) pointed out that the static distribution indices may be normal even in cases with severely abnormal function, if a counter "sees" hyperventilated or hyperperfused alveoli compensating for poorly ventilated or poorly perfused alveoli "seen" by the same counter.

Several authors have assessed regional ventilation from the slope of the wash-in curve during rebreathing of xenon or from the wash-out after equilibration. Bentivoglio et al. (1963a) suggested a dynamic index, using the time needed to reach 90 per cent of the equilibrium counting rate. Recently Glaister (1967) reported the results of a study in which he judged regional ventilation from the slope of the first 30 seconds of the wash-in curve, plotted on a semilogarithmic graph. The counting rate at a pre-determined point on the first steep ascending part of the wash-in curve also proved to be a useful measure of regional ventilation (Arborelius, Fajgelj, Lassen, Lindell, Miörner & Svanberg 1967; Miörner 1967b). Matthews and Dollery (1965) analyzed wash-in and wash-out curves with the aid of an analogue computer. They concluded that more accurate measurements of ventilation can be made from wash-in curves than from wash-out curves, where systemic levels of radioactivity are high and corrections for xenon returning to the lungs from the blood and tissues are difficult to apply. The influence of these mechanisms will be less if only the first part of the wash-out curve is used, as done by Bryan, Bentivoglio, Beerel, MacLeish, Zidulka and Bates (1964) who judged regional ventilation from the time needed to reduce the counting rate to half that of the equilibrium counting rate.

The wash-out rate after intravenous injection of xenon was studied by Dollery et al. (1962). The wash-out curve was plotted on a semilogarithmic graph and the time needed for the counting rate to fall to half was used as a measure of the re-

gional ventilation efficiency. This way of studying regional ventilation was further developed by Heckscher et al. (1966), who performed the investigation with the patient in the supine position. A xenon solution was injected via a needle in the femoral vein, while the patient continued to breathe normally. The regional ventilation was calculated from the wash-out curve according to the formula:

$$\frac{\dot{V}}{V} = \frac{\ln 2}{T_{1/2}} (= k)$$

where $T_{1/2}$ is the half-life of the counting rate measured with external counters. k expresses the regional ventilation per time unit per unit lung volume.

Heckscher et al. (1966) also described another means of calculating the rate of ventilation from the area under the wash-out curve. However, this area may be influenced considerably by xenon dissolved in the chest wall.

A new approach to xenon studies of lung function was presented by Anthonisen et al. (1966) who introduced a method for steady state measurement of regional ventilation/perfusion ratios. Under steady state conditions the concentration of any gas in a lung region is determined by the ventilation/perfusion ratio. During 5 minutes' continuous intravenous infusion of Xe-133 the counting rates over 10 to 12 areas were recorded, when the subject was under steady state conditions. The alveolar xenon concentration was calculated from this data and data obtained under analogous conditions, when the alveolar Xe-133 concentration was known, *i.e.* after equilibrium with a known gas in the spirometer. Bass, Heckscher and Anthonisen (1967) recently reported the results of investigations on patients with pulmonary embolism using the same technique.

Most investigators (e.g. Mannell, Prime & Smith 1966) have accepted the method of measuring *regional lung volume* suggested by Ball et al. (1962), *i.e.* from the external counting rates after rebreathing to equilibrium in a closed circuit containing Xe-133.

(2) *The technical equipment.*

Ball et al. (1962) used scintillation counters on the dorsal side of the chest. Heckscher et al. (1966) counters on the ventral side.

As early as 1958 Dyson, Hugh-Jones, Newbery and West used paired detectors directed towards the same zone of the lung from the ventral and the dorsal sides in $^{15}\text{O}_2$ -studies. Dollery et al. (1962) adapted this arrangement to xenon studies. The impulses from two detectors in a pair were added and recorded together. The contribution to the counting rate was thus fairly uniform from the cylinder of lung tissue between the two detectors.

If it is wished to study several different lung areas simultaneously, a large number of detectors are needed. An attempt to obtain the same information with only four detectors was exemplified by the scanning technique described by Dollery and Gillam (1963). They used two pairs of detectors placed opposite each other, with cir-

cular collimators mounted on a movable metal frame. The movement of the frame was controlled hydraulically. The scanning was performed from base to apex in six seconds. In this way it was possible to acquire an "activity profile" for each lung after injection of xenon, after a tidal breath and after rebreathing from a spirometer with xenon. By comparing these curves, the ratios for ventilation/volume, perfusion/volume and ventilation/perfusion could be determined for different levels of the lung. Dynamic ventilation indices were determined in a similar way by repeated scanning procedures during wash-in and wash-out courses. Glazier and DeNardo (1966) used a similar technique for examining a group of healthy subjects in different body positions. In order to obtain greater resolution and versatility he used rectangular collimators where each window had a length of 7.1 cm and a width of 1.3 cm. Such a narrow collimation requires a relatively high amount of radioactivity, *i.e.* greater exposure to radiation, and consumes more xenon.

In Ball's study (1962), as in most studies from the same institute, the pulse discrimination level was 25 keV. Some authors, *e.g.* Dollery et al. (1962) and Heckscher et al. (1966), recommend a higher discrimination level (80 keV) in order to minimize the influence of Compton scatter.

Most authors have used direct writers for recording. Others, *e.g.* Ball et al. (1962) used a multi-channel tape-recorder.

(3) *Presentation of the results.*

In all the studies mentioned above the results of the xenon studies were presented as perfusion, ventilation, volume ratios or wash-in and wash-out data within the areas of the lung "seen" by the detectors. This may of course be sufficient when the intention of the studies is to obtain information about the physiological mechanisms regulating perfusion, ventilation etc.

Although their technique was not primarily designed for comparison with bronchspirometry, the Montreal-group found a good agreement between the Xe-133 measurements and bronchspirometry in three patients (Bates, Kaneko, Henderson, Milic-Emili, Anthonisen, Dollfuss & Dolovich 1966).

Mannell et al. (1966) used a somewhat simpler method for the quantitation of their results. Six lung zones were studied with paired detectors, three pairs over each lung. The counting rate recorded by each pair of detectors at the different procedures of investigation was expressed in per cent of the sum of the activity in all six zones. The ratios ventilation/volume, perfusion/volume and ventilation/perfusion for each zone were calculated from these figures. They did not compare the function of the two lungs as is done in bronchspirometry.

With the scanning technique introduced by Dollery and Gillam (1963), the results are obtained in activity profiles for each lung. From these profiles it should be possible to make a comparison with bronchspirometry. However, to my knowledge no such comparison has been published.

CLINICAL APPLICATIONS

The Montreal-group has, besides studies of physiological regulation mechanisms, also studied the function in diseased lungs. Already in Ball's et al. paper (1962) the results of xenon-studies in cases with pulmonary emphysema, chronic bronchitis and congestive heart failure were presented. Further studies of regional ventilation and perfusion in pulmonary emphysema were carried out by Bentivoglio et al. (1963 b). They found a zonal predominance in 35 of 40 patients studied and concluded that a precise quantitation of regional function in emphysema is a pre-requisite to an intelligent surgical approach to its treatment.

In an investigation of 12 patients with asthma in remission Bentivoglio et al. (1963 a) found that the static distribution index for ventilation and perfusion did not differ significantly from the findings in normal subjects. Analysis of the rates of wash-in of inhaled xenon, however, revealed significant abnormalities in 6 patients. The ventilatory abnormalities were regional rather than diffuse. Dawson, Kaneko and McGregor (1965) studied 15 cases of mitral valve disease by using the technique of Ball et al. (1962). The ratio of upper-to-lower zone blood flow was found to be increased. The increase tended to be greater in the presence of higher pulmonary venous pressure. The observation was interpreted as a result of an elevation of vascular resistance in the lower zones initiated by perivascular edema which in turn should result from elevated pulmonary venous pressure.

Using the technique described by Anthonisen et al. (1966), Bass et al. (1967) studied regional pulmonary gas exchange in patients with pulmonary emboli. The highest regional $\dot{V}_A/\dot{Q}$ found was about 3 or three to four times that in normal regions. As the ventilation within embolized lung regions was not found to be considerably decreased, the modest increase of the $\dot{V}_A/\dot{Q}$ might be due to incomplete occlusion of the embolized artery or to dead space gas containing Xe-133 being inhaled in the lung regions without blood flow.

At Hammersmith Hospital, London, Dollery et al. (1962) studied the patients with mitral stenosis and pulmonary hypertension and found a higher blood flow through the upper zones. Dollery and Gillam (1963) studied patients with emphysema and bronchitis and patients with mitral stenosis, using scanning technique. In the latter group of patients they found a blood flow per unit volume four times higher in the upper part of the lung than in the lower, while ventilation was evenly distributed.

Larsen and Buemann (1967) studied regional lung function in patients before lung surgery with the technique described by Heckscher et al. (1966). The authors stress the importance of such studies for planning lung surgery, especially in cases with decreased total lung function.

No serious attempt has, however, been made to validate the results of Xe-133 studies by comparing them with bronchspirometry.

Chapter II

CHOICE OF RADIOSPIROMETRIC TECHNIQUE FOR COMPARISON WITH BRONCHOSPIROMETRY

(1) Choice of tracer.

As the purpose of this study was to estimate the regional perfusion, ventilation and volume, only gaseous tracers could be considered. Out of the nuclids used earlier for this purpose, ^{15}O and its compounds could not be considered, since its half-life is so short that it is necessary to have a cyclotron in the immediate vicinity. Most of the radiation given off by ^{85}Kr is too weak to allow external counting. Xe-133 has physical as well as chemical qualities which make it suitable for the investigations intended, even if a gas with even less solubility in blood and tissue would be preferable.

(2) Detectors in fixed relation to the patient versus scanning.

The easiest way to obtain good anatomical resolution with a minimum of equipment should be to use scanning with a narrow collimator. This would, however, require much larger amounts of xenon than with fixed detectors, and would, nevertheless require fairly long breath-holding periods.

Fixed detectors were preferred to the scanning procedure for the following reasons:

(1) The investigation can be carried out with very little active cooperation from the patient and is consequently not very tiring. By modifying the procedure somewhat it can even be carried out without the patient's active cooperation and can therefore be performed also on unconscious patients.

(2) Studies of dynamic events, such as wash-in and wash-out of radioactive gas in the lungs, are easier to perform with fixed detectors and the calculations are simpler.

(3) Position of the subject.

The investigation was carried out with the subject in the supine position for the following reasons:

(1) In the supine position the perfusion is more evenly distributed in the lungs than in the upright position. An apical reduction of perfusion can therefore more easily be revealed when examining the patient in the supine position.

(2) It is easier to keep the position of the subject unchanged in relation to the detectors when he is lying down.

(3) An investigation in the supine position is more comfortable for the subject and can therefore be carried out even in patients who are severely ill.

(4) Number and position of the detectors.

The number of detectors is not only an economic problem. In addition, a great number of recording channels would produce so much data that data-analysis becomes a problem. Heckscher et al. (1966) used only one detector for each lung, whereas Mannell et al. (1966) used 6 detectors for each lung. Even with a large number of detectors it is impossible to obtain a perfect anatomical correlation to the various lobes of the lungs. The primary purpose of the present investigation was to obtain measuring conditions comparable to bronchspirometry, *i.e.* conditions which give information about the function of each lung separately. In addition, the possibility of distinguishing between functional losses in the apical and the basal parts of the lungs was desired. For these reasons it was decided to use four recording channels, two for each lung (Fig. 1).

The fairly weak gamma radiation from Xe-133, about 80 keV, will to a large extent be absorbed by the tissues. To obtain a fairly homogenous sensitivity in the counting field it was decided to use paired detectors, such as were first described by Dyson et al. (1958). The counters are the same as those used by Arborelius et al. (1967), but the original circular collimators have been exchanged for asymmetric ones, designed to "see" as much of the lungs as possible, with a minimal overlapping between right and left lung, and between basal and apical fields (Fig. 7).

The subject was placed in symmetric position in relation to the counters as described on p. 37. It is obvious that reliable results cannot be obtained from this fixed arrangement of the detectors in patients with abnormal position of the lungs due to, for example, deformed chest or displaced mediastinum.

(5) Level of discrimination.

The radiation energy of Xe-133 has two maxima, one around 30 keV and one around 80 keV. Both energies can be used for external measurements. If the discrimination is set to accept also the 30 keV radiation the measurements may be made with smaller amounts of Xe-133 with the same statistical precision. However, with this arrangement the amount of scatter radiation should increase and hence the resolution may decrease. On the basis of experiments described on p. 31 it was decided to use a discrimination which accepted only the energy around 80 keV.

(6) *Recording apparatus.*

Direct-writers or tape-recorders from which each channel can be played back later to a direct-writer can be used for the recordings. The former procedure has the advantage of permitting the investigator to see if technically good results have been achieved. If two or more curves coincide on the direct-writer, it might be difficult to identify the curves. Furthermore, at uneven distribution of function the counting rate of one region may be so large that it falls outside the range of the writer. In order to avoid repeating the procedure in such situations, it was decided to combine the direct-writer with a tape-recorder from which each channel could be played back separately with an amplification suitable to the counting rate.

(7) *Reference lung volume.*

For the calculation of ventilation and perfusion indices, as well as ventilation/perfusion ratios, it is essential that the volume of lung tissue "seen" by each pair of detectors remains approximately the same at measurement of perfusion, ventilation and lung volume. The position after a normal expiration (FRC-position) is fairly easy to reproduce and yet within the range of the normal breathing movements.

When studying the perfusion during apnea, the risk that the patient makes a Valsalva-manoeuvre is less during breath-holding at the end of a normal expiration than at full inspiration. The studies of ventilation should be done during normal breathing, *i.e.* at a lung volume close to the FRC-volume. For technical reasons the ventilation was measured at the volume of FRC plus tidal volume.

(8) *Estimation of perfusion.*

The use of Xe-133 in the studies of regional perfusion is based on the fact that xenon has a low solubility in blood and therefore to a large extent passes from blood to alveolar air in the lung capillaries. It is desirable that studies of the distribution of perfusion be made under physiological pressure conditions in the thorax. Very low or high intrathoracic pressure may influence the distribution of perfusion (Mannell et al. 1966). It would be preferable to give the injection during normal breathing entirely without the subject's active cooperation (Heckscher et al. 1966). However, the wash-out of xenon from the alveoli under such conditions starts already at the moment when the first amount of xenon passes from blood to alveolar air, and before the maximal counting rate is reached. Theoretically this ought to lead to an underestimation of the perfusion within well ventilated areas in comparison with the perfusion within poorly ventilated areas. For this reason, it was decided to let the patient hold his breath at FRC-level immediately after injection for 8

to 10 seconds. The "activity plateau" recorded during the apnea is not affected by differences in regional ventilation. Theoretically, also this plateau should be subject to smaller statistical variations than the peak representing the perfusion during maintained normal breathing. However, injections during normal breathing have certain advantages in some situations, *e.g.* when investigating very ill patients who cannot cooperate properly in the investigation. Although injection during apnea was chosen for the routine investigation, it was decided to compare the results from the two methods. The results of this comparison are presented below (Chapter VII).

Irregardless of which procedure of investigation is preferred, it is important to administer the injection in such a way that all the xenon reaches the pulmonary capillaries in a short period of time. This will be achieved, if the solution is injected close to the right atrium via a catheter. If the injection is given into the femoral vein in the groin, the rapid blood flow in the inferior caval vein carries the solution to the heart with sufficient speed. On the other hand, if the injection is given into a peripheral arm vein the arrival of the xenon in the lungs may be spread over too long a time, *i.e.* an apnea period too long for many patients with lung disease would be required to get reliable results. If such an injection is given during maintained normal breathing, the influence of uneven ventilation will increase. No matter whether the injection in a peripheral arm vein is given during breath-holding or during maintained breathing, the recordings may be disturbed by the Xe-133 in the subclavian vein on the side of injection, which also can persist after the maximal counting rate has been reached in the lungs.

In the choice between an injection in the femoral vein and injection in the superior caval vein via a catheter from a cubital vein, the latter was preferred, in spite of the fact that the procedure is somewhat more time-consuming, because the patient can move freely after the catheter has been inserted, and because puncture of the arm vein is usually less disturbing to the patient.

(9) *Estimation of ventilation.*

Several methods for determining the distribution of ventilation have been used. Summarizing, regional ventilation may be judged on the basis of:

(a) the *decrease of counting rate* during wash-out after equilibration with the gas in a spirometer, containing Xe-133 or after intravenous injection of Xe-133, dissolved in saline.

(b) the *increase of counting rate* after inhalation of Xe-133. The counting rate may be measured during breath-holding after a single tidal or a single maximal inspiration. Ventilation may also be judged from the wash-in during rebreathing from a spirometer with Xe-133.

Alternative (a) was abandoned for the following reasons: Records of the wash-out after equilibration may be influenced by the Xe-133 accumulated in the chest wall during the rebreathing period and by Xe-133 returning to the lungs from the blood and tissues (Matthews & Dollery 1965).

Studies of the wash-out after intravenous injection of xenon provide information mainly about the ventilation of perfused alveoli, but not about the total regional ventilation, and, consequently, do not render the same information as bronchspirometry. The agreement with bronchspirometric results has been found to be less satisfactory (Arborelius et al. 1967).

In reality, both these methods measure ventilatory efficiency and are closer related to nitrogen wash-out in a common lung function test than to the measurement of tidal volume. Studies of the wash-out curves can, however, give important information about the existence of badly ventilated parts within a counting field.

Alternative (b). Breath-holding after inhalation of a tidal breath is a manoeuvre not always easily performed by untrained subjects. Furthermore, with the xenon concentration which is generally used, the counting rate will be low and, consequently, the influence of the random error large (Ball et al. 1962). The distribution of gas after a maximal inspiration depends on the compliance and less on the airway resistance, which might be of importance to the distribution of ventilation during normal breathing. This has been emphasized by Ball et al. (1962) in studies of emphysematous patients.

The wash-in during rebreathing in a closed circuit containing Xe-133 may be utilized for ventilation studies in different ways. Bentivoglio et al. (1963 a) based the determination on the time needed to reach 90 per cent of the equilibrium counting rate. If some parts of the lungs are poorly ventilated, the equilibration time will be long and the contribution of the radiation from the chest wall large enough to interfere with the results.

In a recent study Glaister (1967) used the first 30 seconds of the wash-in curve to assess the regional ventilation. The calculations, including plotting of the curve on a semilogarithmic graph, are, however, more time-consuming than the method used in the present study.

The wash-in of xenon as well as the wash-out are exponential functions and give information about the regional ventilatory efficiency. The quantity best suited for comparison with ventilation, as measured during bronchspirometry, would be the counting rate recorded after inhalation of one tidal volume during normal breathing without breath-holding. For suitable counting rates to be obtained after inhalation of a tidal breath, however, high concentration of Xe-133 is required in the spirometer. The first steep ascending part of the wash-in curve is only to a small extent influenced by the exponential character of the function. There should thus be no theoretical objection to using the counting rate after the third breath as a measure of regional ventilation. At the peak of the third inspiration a suitable counting rate is reached in most cases, even with moderate concentration of Xe-133 in the spirometer

gas (about 0.2 mCi per litre). The systemic levels of radioactivity are still minimal and the spirometer gas has not yet been diluted to any significant extent by the air in the lungs. In order to keep the same lung volume, as at the determination of perfusion and FRC, the peak of expiration should be used. The random error, however, proved to be larger when the peak of expiration was used, compared with the peak of inspiration. For this reason, the peak of inspiration was preferred in spite of the lung volume's deviating somewhat from the reference volume at that moment. No systematic difference was observed between the distribution of ventilation evaluated at the peak of expiration and that evaluated at the peak of inspiration.

(10) Estimation of lung volumes.

The technique introduced by Ball et al. (1962) was used with some small modifications. After some minutes' rebreathing from the spirometer, the air in the lungs at the moment of connection is mixed with the gas in the spirometer. The carbon dioxide eliminated from the lungs is removed by a CO₂-absorber and the O₂ taken up by the lungs is continuously replaced, so that the gas volume in the spirometer is kept constant. It is assumed that the wash-in is complete when the external counting rates have become stable, *i.e.* that the Xe-133 concentration is equal in the spirometer and in all parts of the lung. In this situation the counting rate recorded for one part of the lung is proportional to the volume of gas in the same part of the lung, *e.g.* when reading the counting rate at the end of a normal expiration to regional FRC.

During the wash-in procedure, some xenon is absorbed by the blood in the lungs and is transported to different tissues in the body, including the chest wall. As the chest wall is of approximately the same thickness in the different fields, but the lung volumes generally are much smaller within the apical fields, the Xe-133 in the chest wall will exert a relatively greater influence on the apical fields than on the basal fields, even under normal physiological conditions. It may exert a greater influence on the determination of regional lung volumes in pathological states with great differences in volume in different regions, and this influence will increase with the time required to reach equilibrium.

Milic-Emili, Henderson, Dolovich, Trop and Kaneko (1966) reported a method to correct the counting rates for the chest wall radiation. When the equilibration was completed the subject was disconnected from the spirometer and hyperventilated maximally to clear the lung of Xe-133 as rapidly as possible. Then the counting rates were recorded for 10 to 20 minutes. The contribution from the chest wall at the end of the rebreathing period was determined by back extrapolation. This value was interpolated with the counting rate at the beginning of the rebreathing, thus permitting estimation of the contribution from the chest wall at any moment during the rebreathing procedure. Such corrections have not been used in the present study for the following reasons: The amount of Xe-133 in the chest wall increases rather slowly and

if the rebreathing time is limited to 5 minutes, the clinical importance of the chest wall radiation will be rather small (Milic-Emili et al. 1966). Furthermore, if badly ventilated regions are present, all the xenon will not be washed out from these regions during a short period of hyperventilation, which may lead to an overestimation of the contribution from the chest wall. Thus in cases where a rebreathing period longer than 5 minutes would be desirable, this method of correcting for chest wall radiation is less reliable.

Under the conditions prevailing during the determination of FRC, a change of lung volume is accompanied by a change in the counting rate recorded, which is assumed to be proportional to the change of lung volume (Ball et al. 1962). Determination of the distribution of vital capacity is based on this condition. Regional vital capacity is calculated from the difference in regional counting rates between maximal expiration and maximal inspiration. Since these determinations are not carried out at the reference volume, the parts of the lungs studied at the determination of vital capacity will not be equal to the parts in which perfusion, ventilation and FRC were determined.

Regional vital capacity might be considered as a determination of regional compliance, provided the change in intrathoracic pressure is the same in all regions. This is probably not true (Milic-Emili, Mead & Turner 1964), but in the supine position the differences in intrapleural pressures are small.

Chapter III

METHODS

THE TRACER

Xe-133 is an inert gas with low solubility in the body fluids. The Bunsen coefficient for water is 0.084 and for human whole blood 0.149 ± 0.006 according to Muehlbaeher, DeBon and Featherstone (1966). The solubility in fat is considerably higher than in blood. Conn (1961) gives a partition coefficient fat/blood of approximately 8, brain/blood of approximately 1 and significantly lower ones for other body tissues.

Xe-133 is produced as a fission product by neutron bombardment of $^{235}\text{Uranium}$. The isotope Xe-133 decays to stable cesium, emitting β -particles of a maximum energy of 347 keV. The half-life of Xe-133 is 5.27 days. The β -particles are absorbed by less than 1 mm of tissue. The nucleus formed by β -decay reaches a stable state either by emitting gamma ray of an energy of 81 keV, or by the process of internal conversion, which is accompanied by the emission of X-rays of an energy of approximately 30 keV (Ball et al. 1962).

Once a week Xe-133 dissolved in saline was delivered to the laboratory *). The liquid was transferred to a glass syringe from which the desired amounts could be sucked out into smaller syringes via a two-way cock. The ampules and the syringes used for storing the xenon were kept in lead containers with walls of 5 mm thickness.

Radiation doses: Lassen (1964) gives the following tissue radiation doses with inhalation of a gas containing Xe-133 in a concentration of 1 mCi per litre during one minute, or injection of 5 mCi Xe-133 intravenously:

tracheal mucosa	96.8 mrad
lung	17.5 mrad
gonades	1.1 mrad

Based on these figures, a routine examination, according to the above mentioned procedure, *i.e.* including injection of 0.5 mCi xenon, and, at the most, 5 minutes' rebreathing from the spirometer with about 0.2 mCi/litre, would give the following doses:

tracheal mucosa	approximately 110 mrad
lung	approximately 20 mrad
gonades	approximately 1.2 mrad

*) From the Radiochemical Centre, Amersham, England, or from AB Atomenergi, Studsvik, Sweden.

According to the International Commission on Radiological Protection (ICRP), the highest weekly dose allowed for personnel in radiological work for most organs is 300 mrad and for the gonades 100 mrad.

PRESENTATION OF THE RESULTS

The anatomy of the lungs makes it impossible to study the individual lobes or segments with external detectors. In normal subjects and with the arrangement of the detectors used in this study, the apical fields include the upper lobe and the apical segment of the lower lobe of both lungs. Consequently, the basal fields include the rest of the lower lobe of both lungs and the middle lobe of the right lung. Of course, this is not true if there is any pathological derangement of the lung anatomy, as after lung surgery, in cases with atelectasis and in cases with large emphysematous bullae.

A routine radiospirometry includes these procedures (see also Fig. 1 and Symbols and Abbreviations on pp. 5—6):

- (1) Recording of the background counts.
- (2) Intravenous injection of Xe-133 for estimating the distribution of perfusion.
- (3) Rebreathing from a spirometer with an air-xenon mixture for estimating the distribution of ventilation, functional residual capacity and vital capacity.

There is a linear relationship between the radiation and the deflection of the record line within the range of counting rate used here. It is thus possible to state the amount of radiation from each field in counts per time unit at any moment of the investigation. For determination of the distribution of function it is, however, more convenient to use the linear measure, *i.e.* the vertical distance between the background line and the record line, corrected for differences in the sensitivity of the channels as described on page 36. These quantities are symbolized as shown in Figure 1.

The external counting rates are determined by the volume of the lung in the field, and the concentration of Xe-133 in the lung, and also by the chest wall's absorption for example. Thus the primary data has significance only when compared with one another. The first step in handling the primary data was to express the counting rate in each field as the percentage of the sum of the counting rates in all four fields, as suggested by Mannell et al. (1966). These quantities are indicated by the following symbols:

for the perfusion Q I — Q IV

for the ventilation V I — V IV

for the functional residual capacity FRC I — FRC IV

for the vital capacity VC I — VC IV

and calculated thus:

$$Q I = \frac{Q 1}{Q 1 + Q 2 + Q 3 + Q 4} \times 100$$

The relationship between the apical and basal fields is normally subjected to great individual variations due to differences in the chest geometry. There is, however in normal subjects a rather constant relationship between corresponding parts of the two lungs and also between the perfusion, ventilation and lung volume within each field (Mannell et al. 1966; Heckscher et al. 1966).

To enable a comparison with bronchspirometry (p. 43), it was decided to use the sum of function in the apical and in the basal field (*e.g.* Q II + Q IV) of each lung as a measure of the function of the lung, *e.g.*

$$QR = Q II + Q IV, \text{ i.e. } \frac{Q 2 + Q 4}{Q 1 + Q 2 + Q 3 + Q 4}$$

Similarly VR was used as a measure of the right lung's part of the total ventilation, and FRCR and VCR as a measure of the right lung's part of the total FRC and VC, respectively.

In order to compare the apical fields with each other, the function of the right apical field is also given in per cent of the "total" function of both apical fields, *i.e.*

$$QRa = \frac{Q 2}{Q 1 + Q 2} \times 100$$

The basal fields are compared in a similar way. This was preferred to forming a quotient Q 1 / Q 2 as done by Heckscher et al. (1966).

The relationships between perfusion and volume, ventilation and volume, and between the perfusion and ventilation within each field are symbolized as follows:

Perfusion index (ind. Q I — Q IV) : the relation between perfusion and func-

tional residual capacity in a counting field, *e.g.* ind. Q I = $\frac{Q I}{FRC I}$

Ventilation index (ind. V I — V IV) : the relation between ventilation and func-

tional residual capacity in a counting field, *e.g.* ind. V I = $\frac{V I}{FRC I}$

Ventilation/perfusion ratio (V/Q I — V/Q IV) : the relation between ventilation

and perfusion in a counting field, *e.g.* V/Q I = $\frac{V I}{Q I}$

It must be stressed that the V/Q is not identical with the usual ventilation/perfusion ratio ($\dot{V}A/\dot{Q}$), as neither the magnitude of the alveolar ventilation nor the regional perfusion is known.

DESCRIPTION OF THE APPARATUS

Eight scintillation detectors (TSD 1. Nukleonikinstrument AB, Göteborg, Sweden), are mounted in two horizontal frames facing each other. Each of the counters in one frame is placed opposite one of the counters in the other frame (Figs. 2 and 3). The detectors in such a pair are directed towards the same region of the lung. The sodium

iodide crystals of the counters are enclosed in cylindrical lead collimators, the free end of which is partly covered by a lead plate, which screens the crystal from radiation from adjacent fields (Fig.4). The wooden examination table is covered with a thin foam-plastic mattress. There are two windows in the table, 380×160 cm,

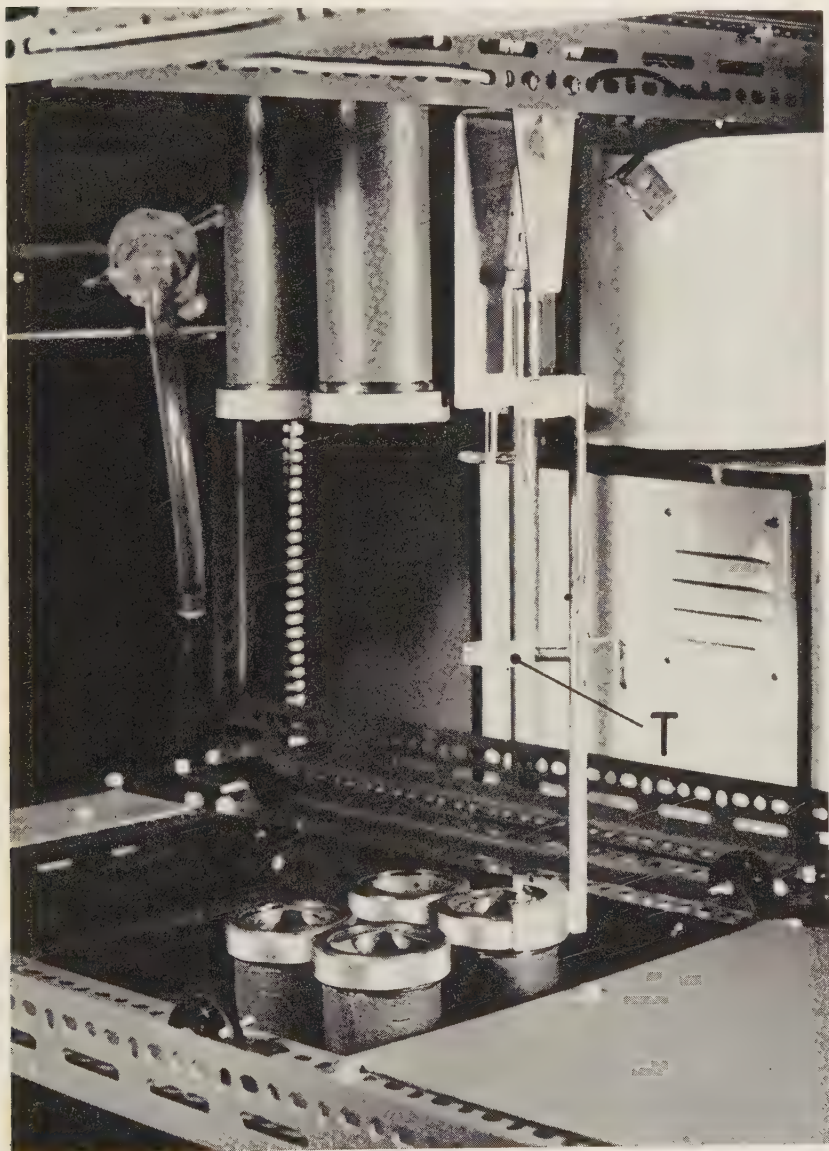


Fig. 2. Arrangement of the detectors. T indicates the test source, p. 36.

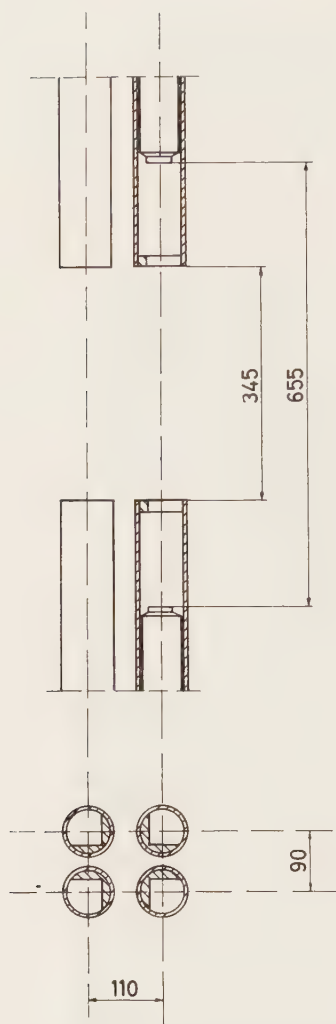


Fig. 3. Sketch indicating the placement of the detectors in relation to each other. Measurements in mm.

corresponding to the lungs of a tall subject. The subject lies down comfortably on the examination table, which afterwards is wheeled into a correct position in relation to the counters. Two spot-lights placed on the centre line facilitate the correct placement of the subject sideways and make it easy to ascertain that the subject has not changed his position during the examination. The examination table is adjusted hydraulically in vertical direction so that the chest of the subject is located half-way between the upper and lower detectors.

The subject breathes through a rubber mouth-piece which is connected via an angle bracket with a one-way valve to plastic tubes having an inner diameter of 22 mm. With the aid of two three-way cocks one of the following alternatives can be chosen:

(1) Inhalation of room-air and expiration into a Douglas bag placed at a distance of 3 m from the examination table.

(2) The inhalation and expiration tubes connected to the spirometer (Pulmotest Godart Amersfoort, Becker Ltd., Delft, Holland). There is a lead jacket around the bell. A pump circulates the gas. Carbon dioxide is absorbed and oxygen is added to keep the gas volume constant during the rebreathing procedure.

The sodium iodide crystals in the detectors have a diameter of $1\frac{1}{2}$ " and are 1" thick. Each of the two high voltage sets (HVS 1500 B, Nukleonikinstrument AB, Sweden) feeds four counters with high voltage (approx. 1300 V).

The recording apparatus (Nukleonikinstrument AB, Göteborg, Sweden) (Fig. 5) includes an amplifier and a discrimination unit. The latter converts all impulses exceeding a pre-set level into impulses of equal magnitude. Pulses of lower energy are excluded. The pulses from the detectors in each pair are totalled in a pulse addition unit. Thus, four channels are formed. The pulses are transferred via four ratemeters to an ultraviolet recorder (Honeywell Visicorder 906 S, Heiland, Colorado, USA), where all four channels are recorded simultaneously, and to a tape-recorder. The rate-

meters can be adjusted to different time constants (in this study approx. 0.6 sec.) and different degrees of amplification.

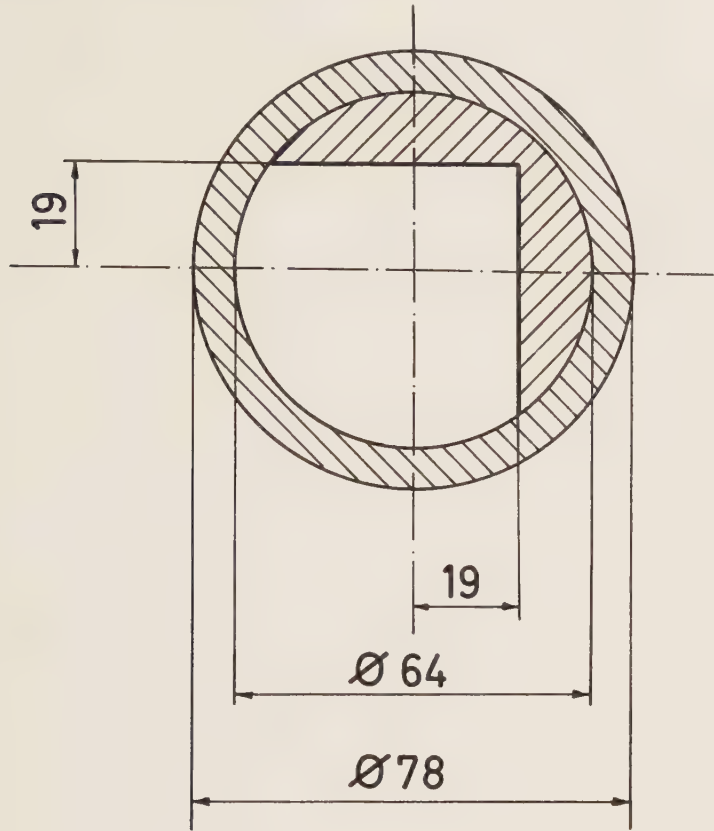


Fig. 4.
Detailed illustration showing the open end of a collimator. Measurements in mm.

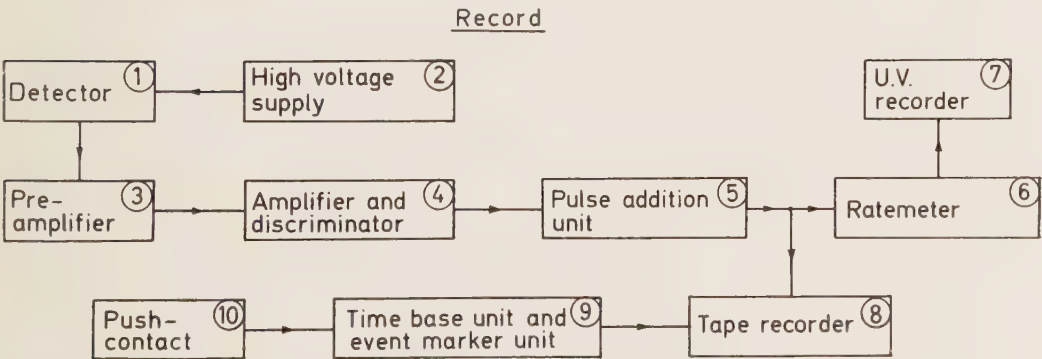


Fig. 5. The record unit. The counting rates are recorded on the ultraviolet recorder (7) and the tape-recorder (8).

Four channels on the tape-recorder are occupied by pulses from the counters. One channel is utilized for manual event marking and one channel for a time base signal with a frequency of 100 p/sec.

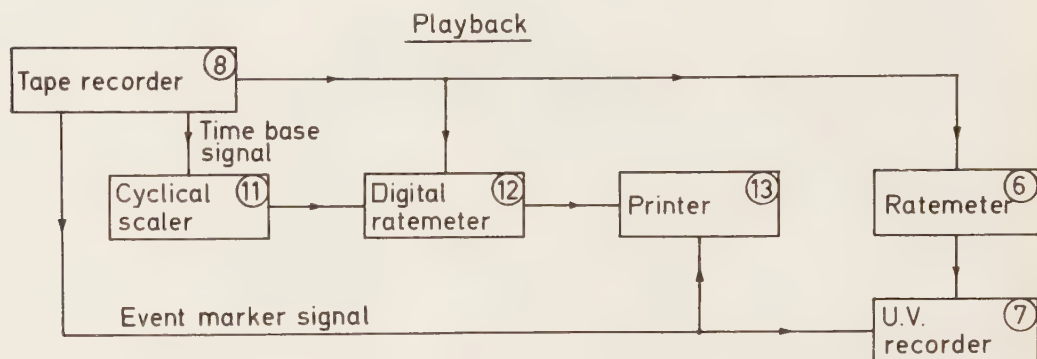


Fig. 6. Playback from the tape-recorder to the printer (13) and to the ultraviolet recorder (7).

Each of the channels with recordings from the counters can be played back separately to the recorder via one of the ratemeters (Fig. 6). The manual event markings are directly transferred to the recorder. From the tape-recorder it is also possible to play back to a digital ratemeter, consisting of two calculators, which alternately count the impulses during the desired time interval. When one calculator is working, the other one delivers the result of the addition made during the previous period to the printer. The length of the period (in this study 5 sec.) is adjusted on the cyclical scaler which is governed by the time base signal from the tape-recorder. The manual event markings are also recorded on the printer.

STUDIES ON THE PROPERTIES OF THE RECORDING APPARATUS

(A) *The counting fields.* A plastic container measuring 18 cm vertically was placed symmetrically between the counters. The container was filled with sawdust in order to simulate the physical properties of the lung (Dollery et al. 1962). Records were made with a "point" source, a xenon bubble with a diameter of 2 mm in a small glass tube which was put in different positions within the container. In this way isocount lines were constructed.

The counting fields in the horizontal plane half-way between the upper and lower detectors are shown in Figure 7. The four fields cover practically all the lung tissue and there is a minimal overlapping between the right and left lung and a slight overlapping between the apical and basal fields.

In the vertical plane (Fig. 8), sensitivity is greatest close to the ends of the collimators. Sensitivity is, however, rather homogenous within a vertical distance of

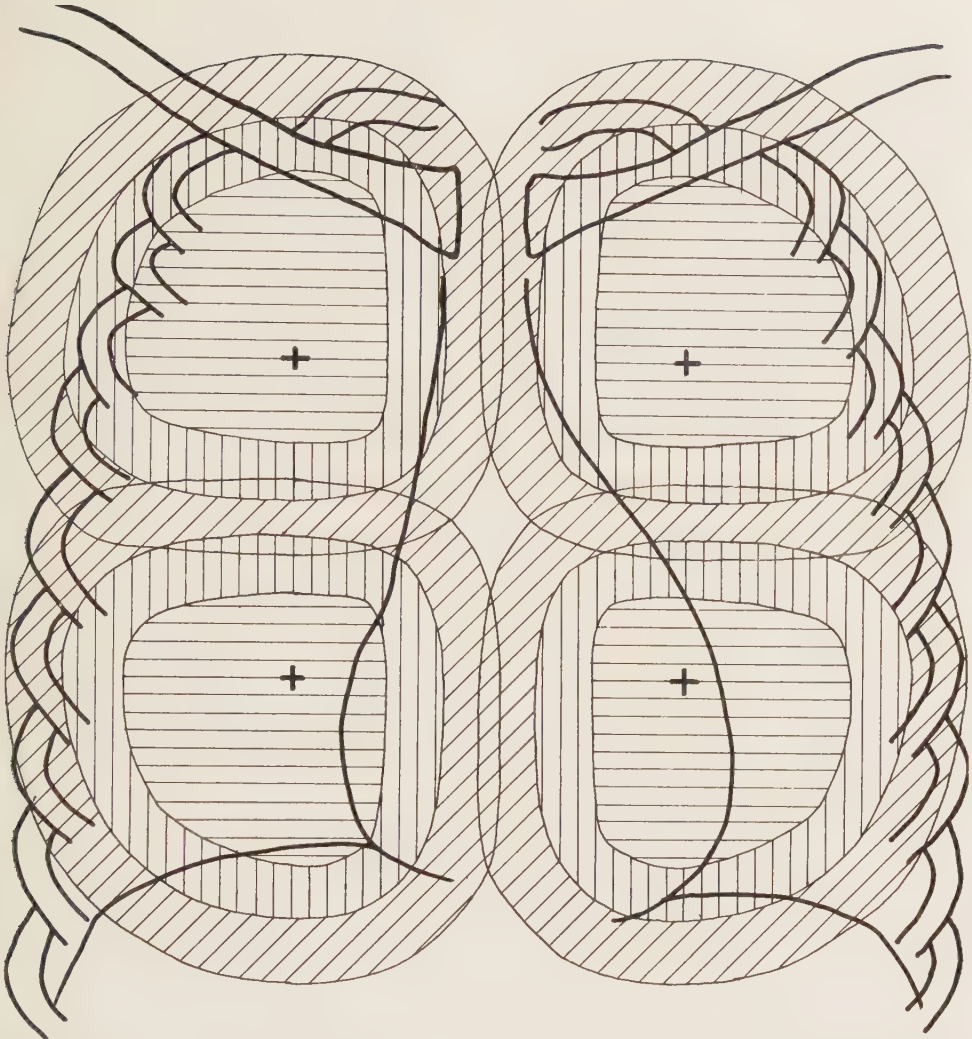


Fig. 7. The counting fields of the detectors in a horizontal plane, half-way between the upper and lower detectors.

- + the optical centre of a pair of detectors.
- ≡ areas with counting sensitivity ≥ 90 per cent of the sensitivity in the optical centre.
- ||| areas with counting sensitivity 50—89 per cent of the sensitivity in the optical centre.
- /// areas with counting sensitivity 10—49 per cent of the sensitivity in the optical centre.

13.5 cm. This means that practically all lung tissue in a person of normal size will fall within the vertical distance with relatively homogenous sensitivity.

(B) Studies of scatter radiation at different levels of pulse discriminations.

If the discriminators are set to accept the weak radiation of xenon with an energy of 30 keV, this will imply a saving of the isotope and a smaller radiation dose for

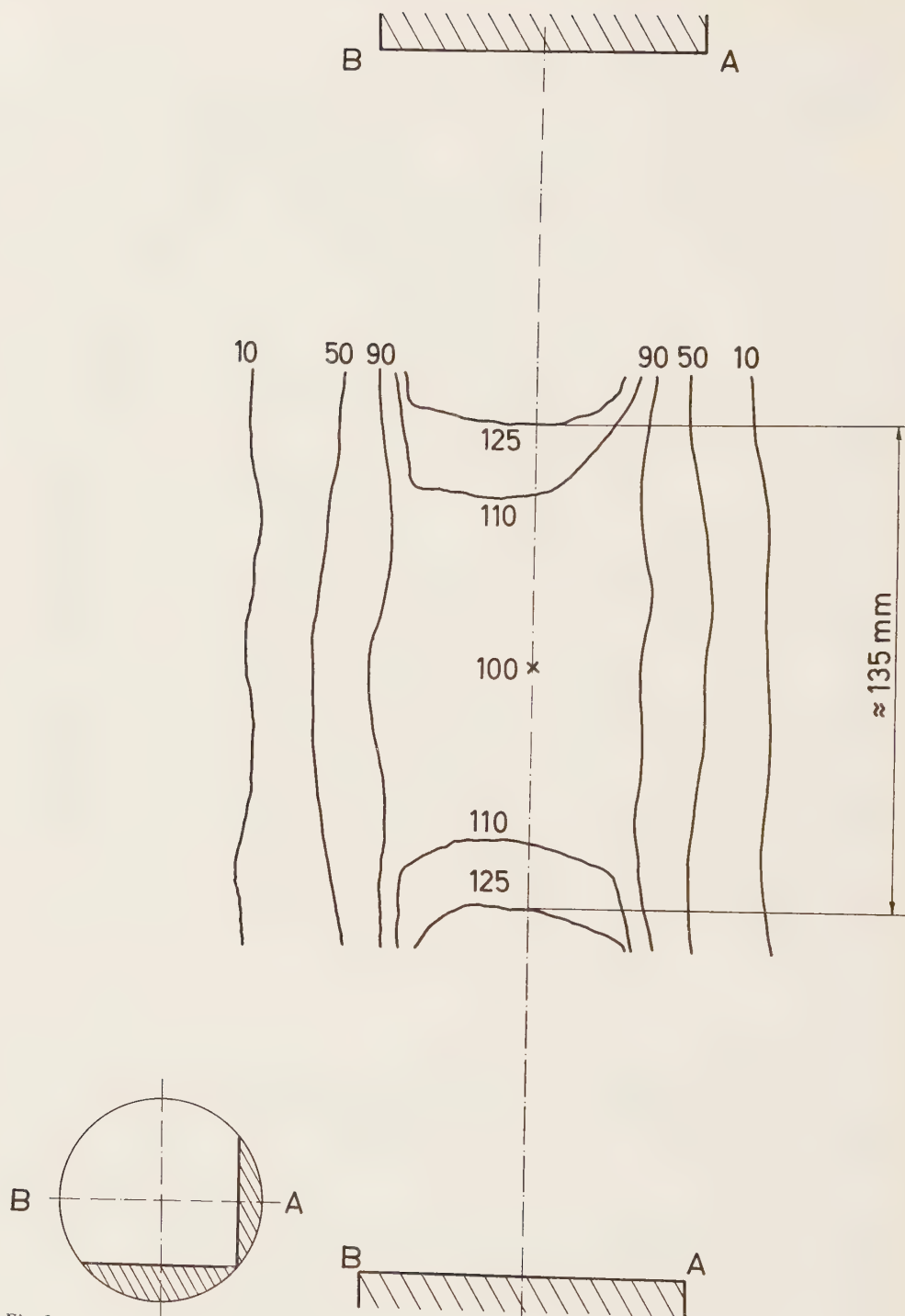


Fig. 8.
Isocount curves for a pair of detectors in a vertical plane, corresponding to line A—B in the small figure. The figures indicate the counting sensitivity in per cent of the sensitivity in the centre.

the patient, but at the cost of precision in the measurements, as more scatter radiation is recorded. The magnitude of this scatter was studied on seven volunteers who were intubated with Carlens' double lumen catheters. The subject was placed on the examination table in the usual way. After some minutes of normal breathing, he was told to make a maximal expiration. One of the tubes was then connected to the spirometer with xenon. The subject was asked to make a maximal inspiration and to hold his breath for 10 seconds. Hereby an "activity level" was reached over the lung with xenon and the counting rate over the opposite lung rose simultaneously. The counting rate recorded over the air-containing lung was assumed to be due to Compton scatter, as the rise of counting rate was synchronous over both lungs and also the fall of counting rate when the subject exhaled. Blood-transported xenon can thus hardly be responsible for the counting rate recorded over the lung with air. The results are summarized in Table 3. The scatter radiation, on the average 7 per

Table 3

Studies of the scatter radiation in vivo.

Counting rates from the lung containing air, in per cent of the counting rates from the lung with Xe-133.

	Discrimination level "75" keV	Discrimination level "25" keV
n	9	9
Mean	3.0	7.1
Range	1.2—3.8	3.8—8.9

cent at a discrimination level of about 25 keV, was regarded as a source of error having clinical importance justifying a choice of a higher level of discrimination, which gave a scatter radiation of approximately 3 per cent, in spite of the arrangements requiring a somewhat higher amount of xenon for the same counting rate.

(C) *Studies on the spatial resolution of the measuring apparatus with the aid of a lung model of acrylic plastic* (Fig. 9).

The "lungs" were connected via a flexible tube. A transverse line over each "lung", half-way between the apex and the base, divided it into one apical part with a volume of approximately 670 ml, and one basal part with a volume of approximately 1330 ml. In each "lung" there was a rubber balloon fastened to a plastic tube going through a rubber stopper at the top of the "lung". The balloon could be filled with the desired amount of gas or liquid via the tube. Via another tube from the side of one of the "lungs", the corresponding quantity of gas was sucked out from the "lungs" in order to maintain the "lung" pressure unchanged. The "lungs" were fed with Xe-133 in a concentration giving approximately 30.000 cpm over the basal fields and approximately 15.000 cpm over the apical fields. The model was placed

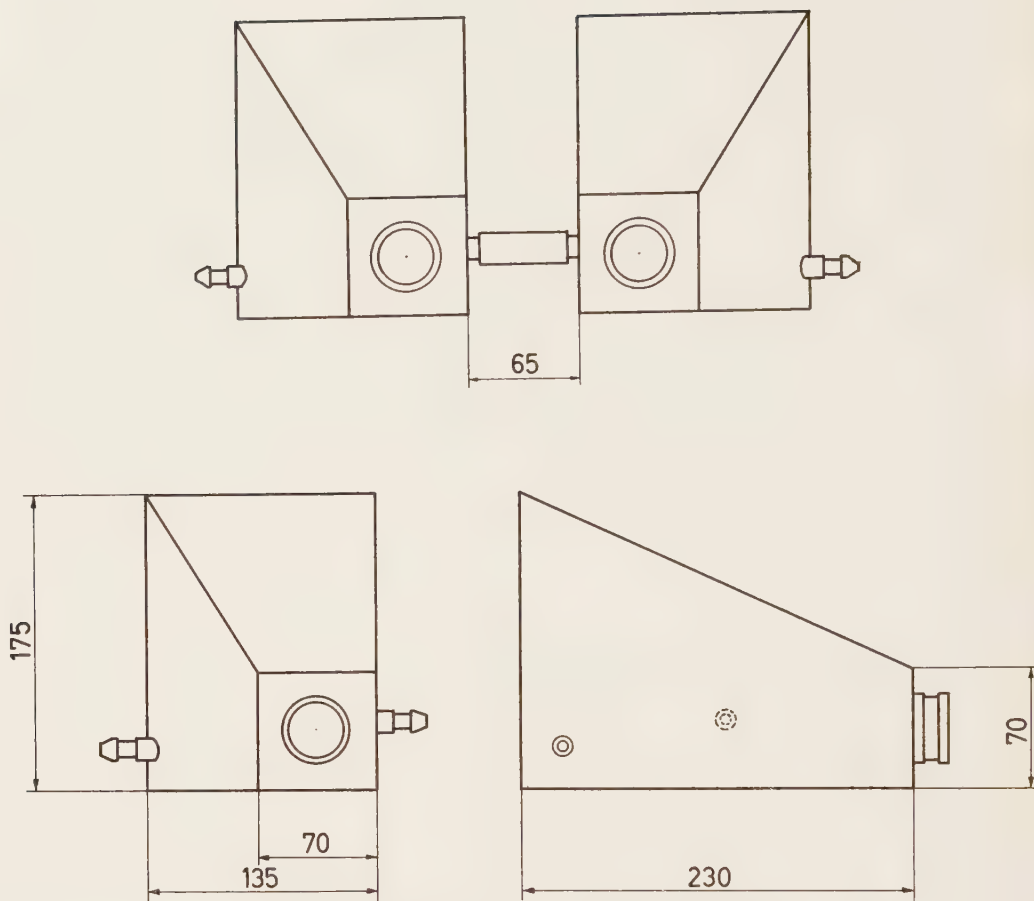


Fig. 9. The plastic "lungs". Measurements in mm.

symmetrically in relation to the detectors, and the results expressed as they were described for human subjects (p. 25). The counting rate was recorded on the tape-recorder for periods of 3 minutes. Each channel was played back via the digital printer.

Due to the long measuring time, the influence of random variations in counting rates was small. In a series of measurements, the error of a single determination judged from duplicate measurements was:

- for the right "lung" (corresponding to FRC *R*): 0.18 per cent
- for the right apical field (corresponding to FRC *Ra*): 0.16 per cent
- for the right basal field (corresponding to FRC *Rb*): 0.24 per cent.

In one experiment the balloon in one "lung" was filled with 200 ml water or 200 ml air. Measurements were performed with the balloon in the right "lung" in the following positions:

Position 1: the balloon placed centrally in the basal field.

Position 2: the balloon placed symmetrically in relation to the transverse line between the apical and basal fields.

Position 3: the balloon placed centrally in the apical field.

The results are reported in Table 4. The figures in parenthesis give the results when the balloon was filled with 200 ml air instead of water. Results of measurements with an air-filled balloon, however, showed less satisfactory reproducibility, probably because of diffusion of Xe-133 through the walls of the balloon.

Table 4

Changes in the distribution of counting rate caused by a balloon filled with 200 ml water or air in different positions in the lung model.

	Right "lung" in per cent of total	Right apical field in per cent of both apical fields	Right basal field in per cent of both basal fields
With empty balloon before the experiment	47.4	48.9	47.3
With the filled balloon in position 1	-5.3 (-3.2)	-0.2	-8.2 (-5.1)
With the filled balloon in position 2	-3.2	-3.3	-2.8
With the filled balloon in position 3	-4.0 (-3.6)	-9.8 (-10.0)	+0.2
With empty balloon after the experiment	-0.2	-0.2	-0.1

The figures within brackets were obtained with air in the balloon.

The decrease in the volume of radioactive gas was:

$$\text{for the entire right "lung"} \frac{2000}{4000} - \frac{1800}{3800} = 2.6 \text{ per cent (positions 1, 2 and 3)}$$

$$\text{for the right base } \frac{1330}{2660} - \frac{1130}{2460} = 4.1 \text{ per cent (position 1)}$$

$$\text{for the right apex } \frac{670}{1340} - \frac{470}{1140} = 8.8 \text{ per cent (position 3)}$$

In all positions the decrease in counting rate over the entire test "lung" was greater than the decrease in gas volume calculated theoretically. This may be due to the balloon's being placed in a "sensitive" volume which contributes to the counting rate more than is average for the entire "lung". At position 1 the difference was greater between the loss of radioactive gas calculated theoretically, and the measured decrease of counting rate. This may be due to the water-filled balloon's screening the detectors from part of the radiation from the gas on the opposite side of the balloon. This mechanism ought to have a greater influence on the counting rate within the basal field, having, as it does, a thick gas layer in the same vertical plane as the balloon. This assumption was supported by the fact that the data obtained with an air-filled balloon was closer to that calculated theoretically. The circumstances attendant to

these measurements are very different from those attending measurements on human subjects. The figures are presented only to demonstrate that the volume of xenon-free matter caused a decrease of counting rate of at least the same magnitude as predicted theoretically from the volume, and that the measured decrease was smaller when the balloon was placed on the border-line between the apical and basal fields, than when it was in the centre of a counting field. With the xenon-free volume in the border-line position, the significance of a measured decrease of counting rate was not greater when the two apical and basal fields were compared, than when the entire "lungs" were compared.

ROUTINE PROCEDURE OF THE INVESTIGATION

Preparations.

(A) Preparation of the apparatus. The sensitivity of the detectors: For adjustment of the sensitivity of the detectors, an acrylic plastic container filled with xenon was used, placed on a stand half-way between the upper and lower detectors (T in Fig. 2). By alternately disconnecting the upper and lower detector, the sensitivity of each detector was adjusted-in, so that the same deflection was obtained from all eight detectors. It was observed that the sensitivity remained almost unchanged for several weeks. In the daily routine check-up, the individual detectors were consequently not tested, but only each channel.

If the differences between the channels were small, the amplification was not re-adjusted, but the results were corrected for differences in sensitivity in the following way: The counting rate from the test source was recorded for one minute on each channel (tape-recorder and digital printer), the counting rates were added and the counting rate from each channel was expressed in per cent of this sum. The counting rates measured on the same day were divided by this figure for each channel. The data corrected in this way was independent of the sensitivity of the counters. If the counting rate of a channel was outside the range 25 per cent $\pm$ 2 per cent of the sum, the sensitivity of the individual counters was re-adjusted.

The spirometer contained approximately 11 litres of air. Xenon solution was gradually injected, until a xenon concentration of about 0.2 mCi/litre gas was reached*). As the spirometer was not equipped with a special counter, the concentration of Xe-133 was checked by placing the plastic tube, through which spirometer gas was pumped, in a fixed position in relation to one pair of counters. Under these circumstances a suitable xenon concentration corresponded to about 6000 counts per minute.

*) This amount refers to the Swedish solution of Xe-133, which in our experience gives 3—4 times higher counting rates than the English solution.

The ratemeter was adjusted so that a full deflection on the U.V. recorder corresponded to 30.000 counts per minute during the investigation of perfusion and ventilation, and to 100.000 counts per minute during the determination of FRC and VC.

(B) Preparation of the subject. The median line of the chest from the incisura manubrii sterni to the xiphoid process was marked on the skin. During fluoroscopy in the supine position, the transverse line half-way between the diaphragm at maximal inspiration and the apex of the lung was drawn using the side with the greatest distance between the apex and the diaphragm. The fluoroscope was equipped with an amplifier and television screen. The radiation dose could thus be kept low. A catheter was inserted percutaneously into a cubital vein using Seldinger's (1953) technique. The catheter was passed to the upper caval vein about 2 cm above the right atrium. A steel leader was used in order to make it possible to check the position of the catheter fluoroscopically. The catheter was provided with a two-way cock, flushed with saline and fixed to the arm. The subject then walked to the examination table and was placed with the chest symmetrical in relation to the counters, *i.e.* with the median line on the skin half-way between the right and the left counters, and the transverse line half-way between the apical and basal ones.

Estimation of regional perfusion.

The subject was carefully instructed about the procedure. When he stopped breathing at the end of a normal expiration, 0.1—0.2 mCi Xe-133 *) in saline solution was rapidly injected, and the catheter immediately flushed with saline solution. The subject held his breath at end-expiratory level for 8—10 seconds and then started to breathe normally. During the first passage through the alveolar capillaries, most of the xenon diffuses from the blood to the alveolar air, and remains there as long as the subject is holding his breath. The counting rates are constant during this period of time, represented on the records by horizontal levels with a length of 2—3 cm. Figure 10 shows the direct record from an investigation of a healthy volunteer. The vertical distance from the plateau to the background line of each channel, after correction for any differences in the sensitivity of the channel, reflects the perfusion within that field, and is used to calculate the distribution of perfusion within the lungs, as described on page 25.

Sources of error: (A) Low activity. The influence of random error increases with low counting rates. For this reason counting rates below 10.000/min. in each channel were not accepted in normal subjects or in patients with moderate functional abnormalities.

*) This amount refers to the Swedish solution of Xe-133, which in our experience gives 3—4 times higher counting rates than the English solution.

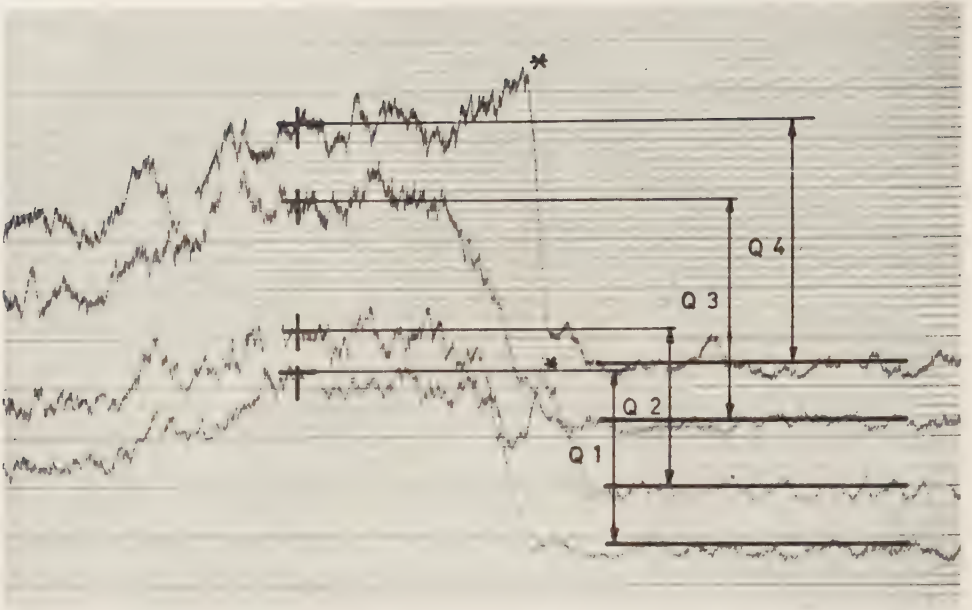


Fig. 10. Record from a perfusion study in a normal subject. (See: Symbols and Abbreviations, pp. 5—6). * represents the counting rate from Xe-133 in the heart and the central blood vessels.

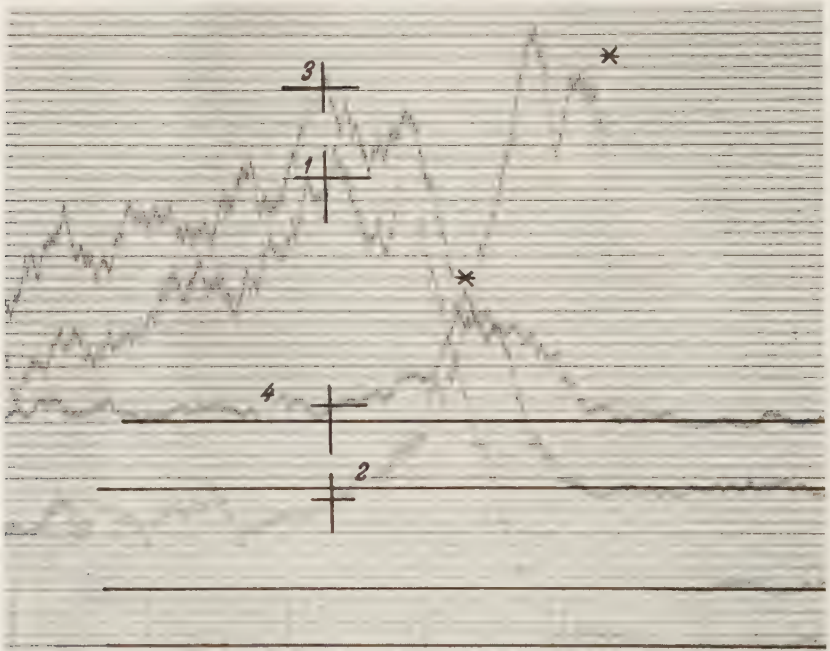


Fig. 11. Record from a perfusion study in a patient after pneumonectomy. The peaks (*) from the pneumonectomized hemithorax are due to Xe-133 passing the heart and the central blood vessels.

(B) Injection artefacts. When the xenon passes the mediastinal vessels and the right heart, it often causes an increase of the counting rate in one or more channels. This radiation is prominent over the pneumonectomized hemithorax in patients after pneumonectomy (Fig. 11). Normally this activity is prior to, or coincides with the ascending part of the curve representing the activity in the lung (* in Fig. 10). It may also deform the first part of the plateau. For this reason, the last part of the plateau, just before the subject starts breathing, was routinely used in all four channels for the calculations. If the blood flow is abnormally low, *e.g.* if the subject makes a Valsalva manoeuvre, or in the presence of congestive heart failure, xenon may persist in the vessels during the whole breath-holding period. The "activity plateau" will be replaced by a down-ward sloping line (Channel 1 in Fig. 12). Such a recording does not allow the estimation of the distribution of perfusion and should be eliminated.

(C) Redistribution of injected Xe-133 during breathing. In cases with very poor perfusion in some areas, an increase of the counting rate can be noticed in the poorly perfused parts, when the patient starts breathing after the apnea. This counting rate is due to inhalation of dead space air with xenon, coming from well perfused areas.

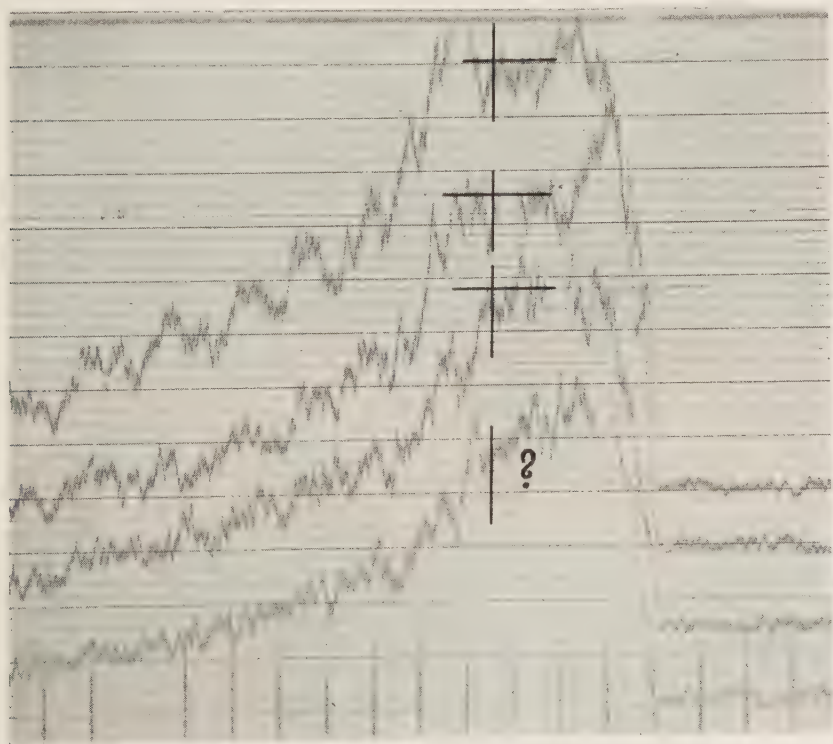


Fig. 12. Record from a perfusion study. The counting rate due to Xe-133 in the heart and central blood vessels cannot be distinctly separated from the counting rate due to Xe-133 in the alveoli in Channel 1.

Figure 13 shows a recording from a patient with pronounced bullous emphysema in the lower lobes. The true perfusion in the basal fields was represented by the level of the curve coinciding with the "activity plateau" of the well perfused areas.

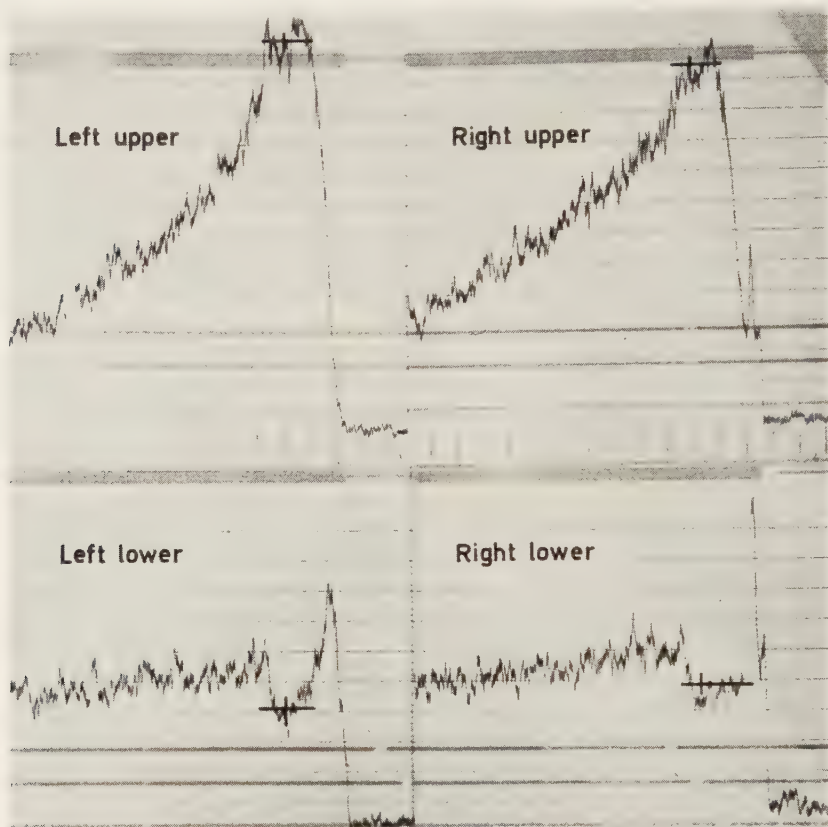


Fig. 13. Record from a perfusion study in a patient with severe bullous emphysema in the basal parts of both lungs. Dark horizontal lines indicate the levels representing the perfusion in the different counting fields.

Estimation of regional ventilation.

As soon as the injected xenon had been washed out, the subject was switched into the closed spirometer circuit. A careful checking was made, to see that the subject was breathing normally at that moment. The counting rate reached at the third inhalation was chosen as representative for the distribution of ventilation. The direct record from a ventilation study in a healthy subject is shown in Figure 14.

Sources of error: (A) Low counting rate. As for perfusion studies, about 10,000 counts per minute in each channel were desired. If the breathing was rapid and shallow, this level was not reached until the fourth breath, which was chosen in such cases.

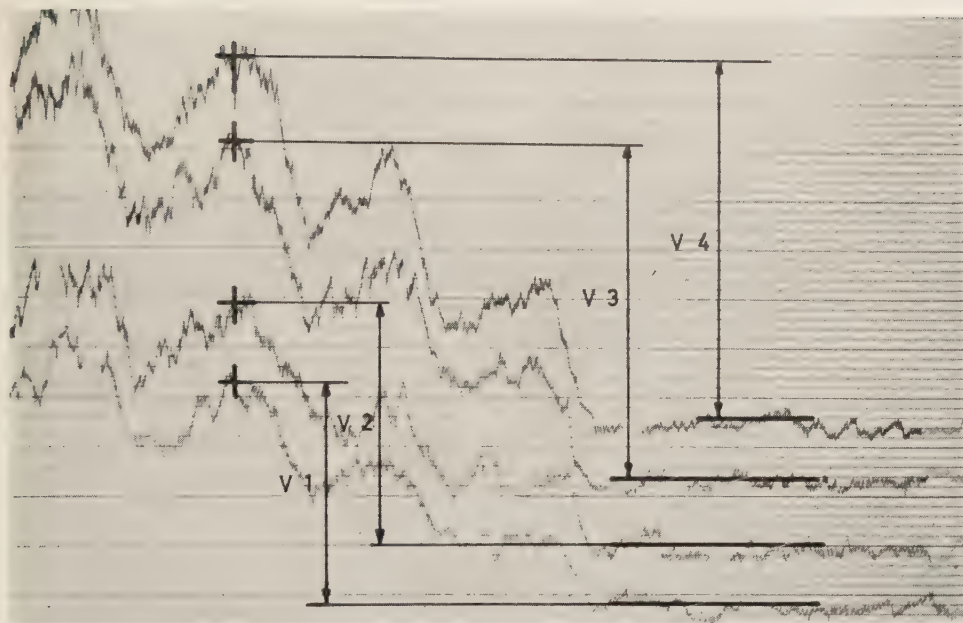


Fig. 14. Record from a ventilation study in a normal subject. (See: Symbols and Abbreviations, pp. 5—6).

(B) Uneven breathing. The accuracy of the determination decreases if the depth of breathing is very uneven. In such cases the investigation was repeated later, when the subject's breathing was relaxed.

If the recording of the third breath was deformed in one or more channels, and the counting rate of the second inhalation was high enough, this was chosen. Comparisons between determinations based on the counting rates at the second, third and fourth inhalation were carried out in a number of cases, and the results were found to be essentially similar.

Estimation of regional lung volumes (FRC and VC).

The rebreathing in the closed spirometer circuit, started at the estimation of regional ventilation, was continued. In order to accelerate the wash-in, the subject was asked to take a few deep breaths several times during the wash-in procedure. After 2 to 5 minutes, stable counting rates were obtained. At that moment, the xenon concentration was assumed to be equal in the spirometer and in all parts of the lungs. The counting rate at the end-expiratory level was assumed to represent the FRC within the field. At the end of the rebreathing procedure, the subject was asked to make a maximal expiration, breathe normally a while and then to make a maximal inhalation. The vertical distance between the peak of expiration and the peak of in-

spiration was assumed to represent the vital capacity in the field. Very often it was difficult to identify the different channels in this part of the direct record. For this reason, each channel was played back separately from the tape-recorder. Figure 15 shows a result from channel 1 in a normal subject.

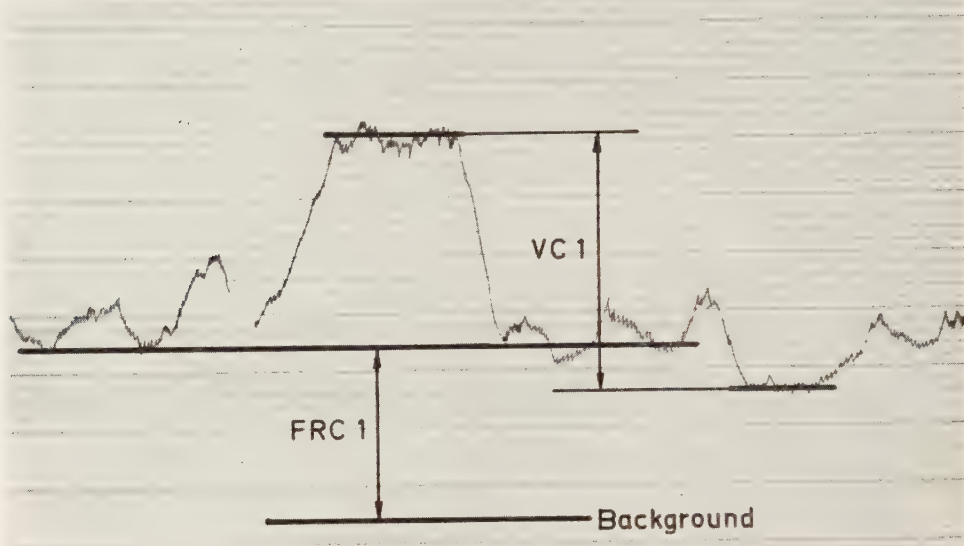


Fig. 15. Record from a study of lung volumes in a normal subject. Channel 1 played back from the tape-recorder. (See: Symbols and Abbreviations, pp. 5—6).

Sources of error: The influence of xenon deposited in the chest wall during the re-breathing procedure has been discussed (p. 22). In order to reduce the radiation dose and to avoid the rather time-consuming correction for xenon in the chest wall, it was decided to limit the rebreathing time to 5 minutes. If there are poorly ventilated parts of the lungs, equilibration will not be completed in 5 minutes, and the estimation of volumes will thus be less accurate. Taking into consideration the disadvantages of longer rebreathing time, this error was accepted in clinical routine work.

Chapter IV

COMPARISON BETWEEN BRONCHOSPIROMETRY AND RADIOSPIROMETRY IN A CLINICAL MATERIAL

Since the aim of the present study was to develop a radiospirometric technique which could replace bronchspirometry, it was decided to compare the results obtained with the technique presented in the previous chapter with those obtained by conventional bronchspirometry in patients with pulmonary disease. Bronchspirometry was performed with the technique described by Svanberg (1957). Only results of examinations in the supine position were used for the comparison. Radiospirometry was carried out as described in Chapter II. If double determinations of ventilation and perfusion were performed, the results from the first determination were used for the present comparison.

MATERIAL

35 patients who were admitted to the laboratory for bronchspirometry were also subjected to radiospirometry. It was preferred to perform the radiospirometry prior to the bronchspirometry and as near in time as possible. If this was not possible, the radiospirometry was postponed until 3 to 4 days after the bronchspirometry, when any irritation of the throat and bronchi had disappeared.

The comparison between radiospirometry and bronchspirometry comprises 35 cases with determination of ventilation and perfusion, 21 cases with determination of FRC, and 29 cases with determination of VC. The material is smaller for FRC and VC, because in the beginning of the study these determinations were not routinely performed in the supine position at bronchspirometry.

RESULTS

The clinical diagnoses and the results of conventional lung function tests are given in the Appendix (Table 1). The results of the bronchspirometric and radiospirometric measurements of perfusion, ventilation and lung volumes are given in the Appendix (Table 2).

The results are also reported in Figures 16—19, where *the function of the right lung in per cent of the total function at bronchspirometry has been plotted against the function at radiospirometry*. In the statistical analyses the bronchspirometric

results have been regarded as accurate. In two cases (represented by points 1 and 2 in Fig. 16) with almost complete obstruction of a main bronchus this was apparently not the case (see below p. 50). The results of perfusion measurement in these two cases (cases nos. 1 and 3 in Table 2, Appendix) were excluded from the statistical analyses.

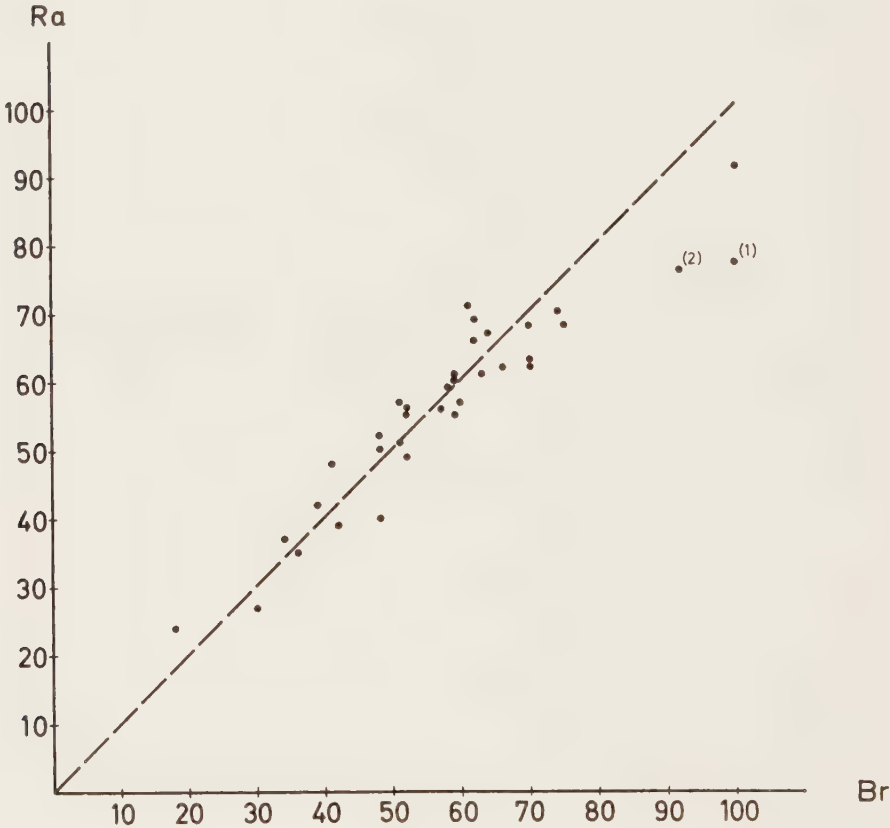


Fig. 16.
Distribution of perfusion in 35 patients with lung disease.
X-axis: the perfusion of the right lung in per cent of the perfusion of both lungs estimated with bronchspirometry (Br).
Y-axis: the perfusion of the right lung in per cent of the perfusion of both lungs (Q R) estimated with radiospirometry (Ra).
The line of identity is represented by the diagonal line.

A linear relationship was presumed between radiospirometry (Y) and broncho-spirometry (X). The regression line:

$$Y = a + b \times X$$

was estimated as the least square regression line (See Statistical Methods p. 6). These regression lines were related to the line of identity as shown in Figures 20—24.

Then the following hypothesis was tested for the different parameters: $a = 0$, $b = 1$, *i.e.* that the regression line is $Y = X$ at the significance level of 5 per cent.

Perfusion

When 33 cases were studied (cases nos. 1 and 3 excluded, Fig. 16), there was a significant difference (***) between the bronchspirometric and the radiospirometric results (Fig. 20).

However, in the 29 cases whose right lung had a relative perfusion of 30 to 70 per cent, there was no significant difference between bronchspirometry and radiospirometry.

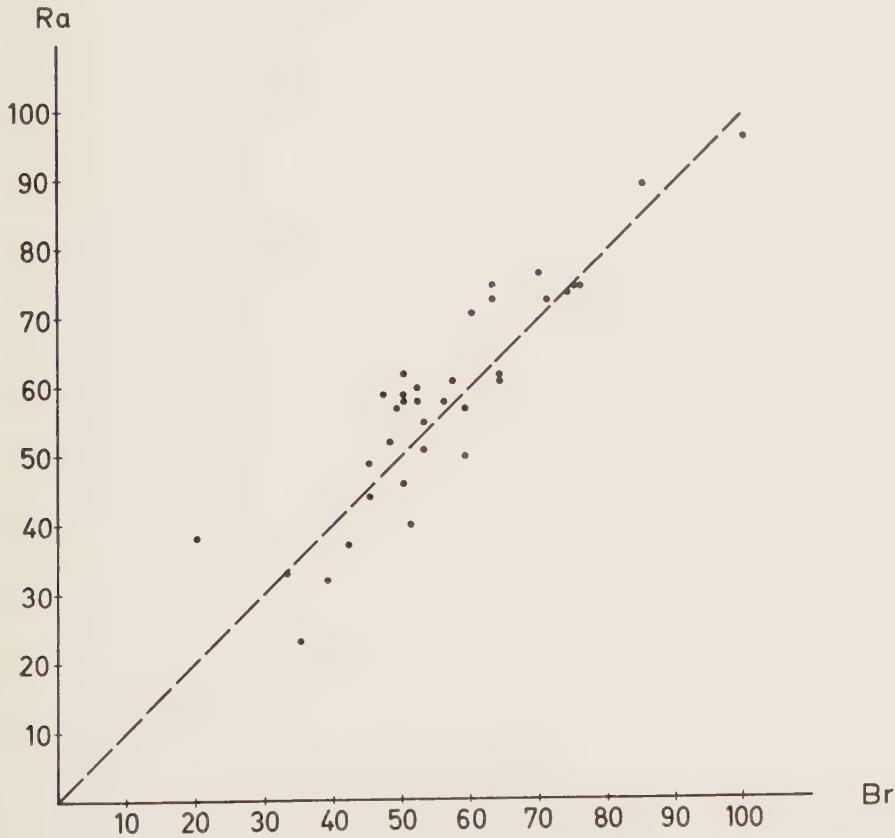


Fig. 17.
Distribution of ventilation in 35 patients with lung disease.
X-axis: the ventilation of the right lung in per cent of the ventilation of both lungs estimated with bronchspirometry (Br).
Y-axis: the ventilation of the right lung in per cent of the ventilation of both lungs (VR) estimated with radiospirometry (Ra).

Ventilation

There was no significant difference between the bronchspirometric and radiospirometric results (Figs. 17 and 22).

Functional residual capacity

In this comparison a significant difference (*) was found between the methods (Figs. 18 and 23).

Vital capacity

For the cases in this comparison there was no significant difference between the methods (Figs. 19 and 24).

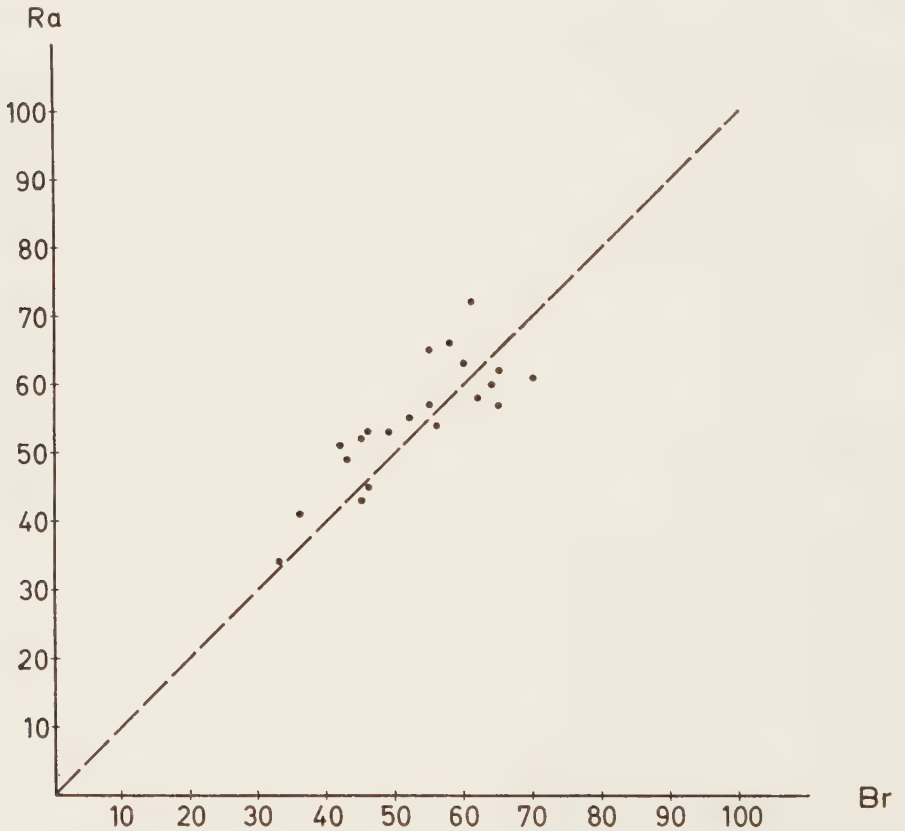


Fig. 18.

Distribution of functional residual capacity in 21 patients with lung disease.

X-axis: the functional residual capacity of the right lung in per cent of the functional residual capacity of both lungs estimated with bronchspirometry (Br).

Y-axis: the functional residual capacity of the right lung in per cent of the functional residual capacity of both lungs (FRC R) estimated with radiospirometry (Ra).

DISCUSSION

Bronchspirometry and radiospirometry represent two fundamentally different methods of measuring the function of each lung separately. Bronchspirometric measurements are based on the flow of gas through the tubes to the two main bronchi. When the subject is examined in the supine position, a loss of function affects the results of the analysis equally wherever it is located in the lung (the pressure gradient in the ventro-dorsal direction being neglected). In radiospirometry, the distribution of function is judged from the distribution of Xe-133 in the lungs, measured by external counters. With the standard method, the radioactivity is not measured with equal sensitivity in all parts of the lung. A functional defect centrally located in a counting field has a greater influence on the results than a

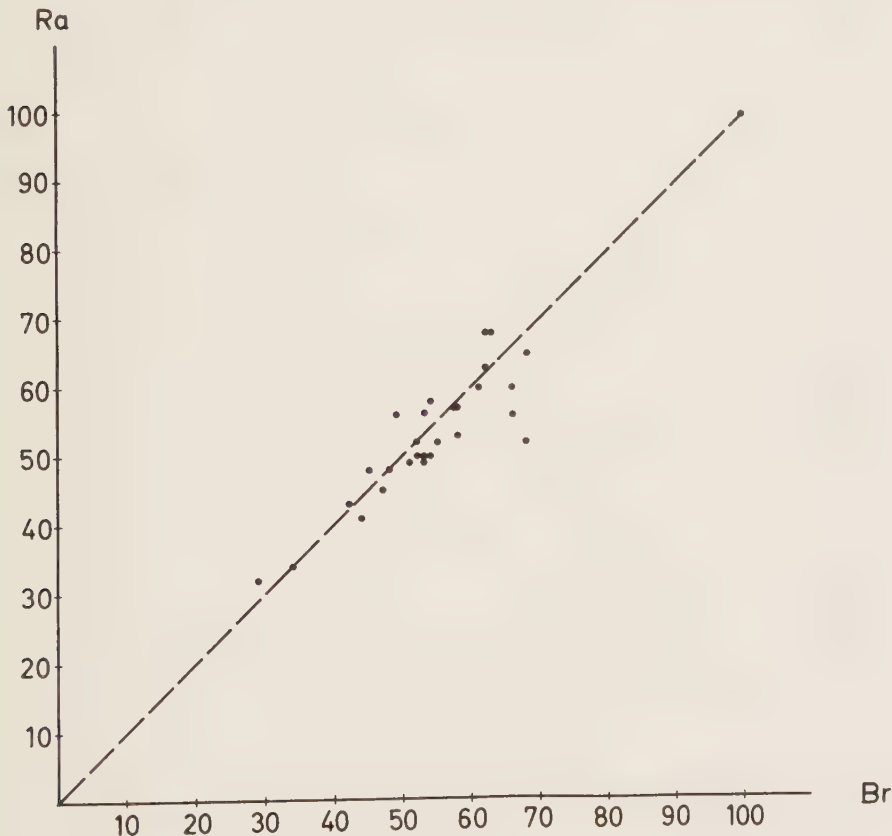


Fig. 19.

Distribution of vital capacity in 29 patients with lung disease.

X-axis: the vital capacity of the right lung in per cent of the vital capacity of both lungs estimated with bronchspirometry (Br).

Y-axis: the vital capacity of the right lung in per cent of the vital capacity of both lungs (VC R) estimated with radiospirometry (Ra).

defect in the border zone between the apical and the basal field, or in the periphery of a field. Judging from the results above, this does not seem to invalidate the results of radiospirometry as compared with bronchospirrometry. Some of the differences found are very likely to have other causes which will be discussed further on.

As is apparent from the position of the regression lines in Figures 20—24 radiospirometry tends to overestimate the function of the most affected lung in comparison with bronchospirrometry. If a lung at bronchospirrometry is found to have no perfusion, ventilation or VC, its function according to radiospirometry, as estimated by extrapolation, is approximately 4.5 per cent. This figure is of the same magnitude as Compton scatter registered over the air-containing lung during unilateral inhalation of Xe-133 (p. 31). During short manoeuvres, such as estimation

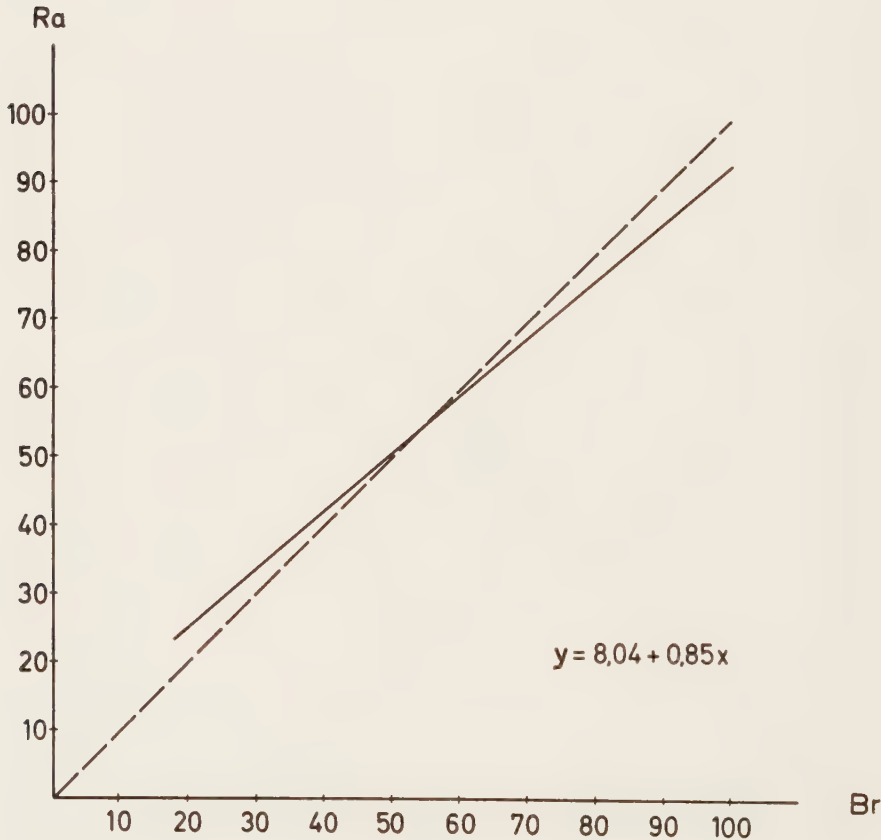


Fig. 20.
Distribution of perfusion in 33 cases. The regression line estimated from the results presented in Figure 16. The subjects represented by points (1) and (2) were excluded from the calculation.

of perfusion and ventilation, it seems that only Compton scatter influences the counting rate over the opposite lung. This is also true for rapid changes in radioactivity, as when studying the VC.

As shown in Figure 23, the volume (FRC) of a poorly functioning lung is overestimated by radiospirometry as compared with bronchosprometry. The explanation is supposed to be the following: During the rebreathing procedure, which lasts several minutes, xenon is taken up by the blood in the lung capillaries and carried to the body tissues, including the chest wall. The counters thus record the radiation from the chest wall, as well as from the lung. As shown in Figure 23, the counting rate over a lung without any demonstrable function at bronchosprometry may be estimated by extrapolation to be 16 per cent according to radiospirometry. One more factor might cause the diseased lung to receive a greater relative FRC according to radiospirometry than with bronchosprometry. In order to shorten the

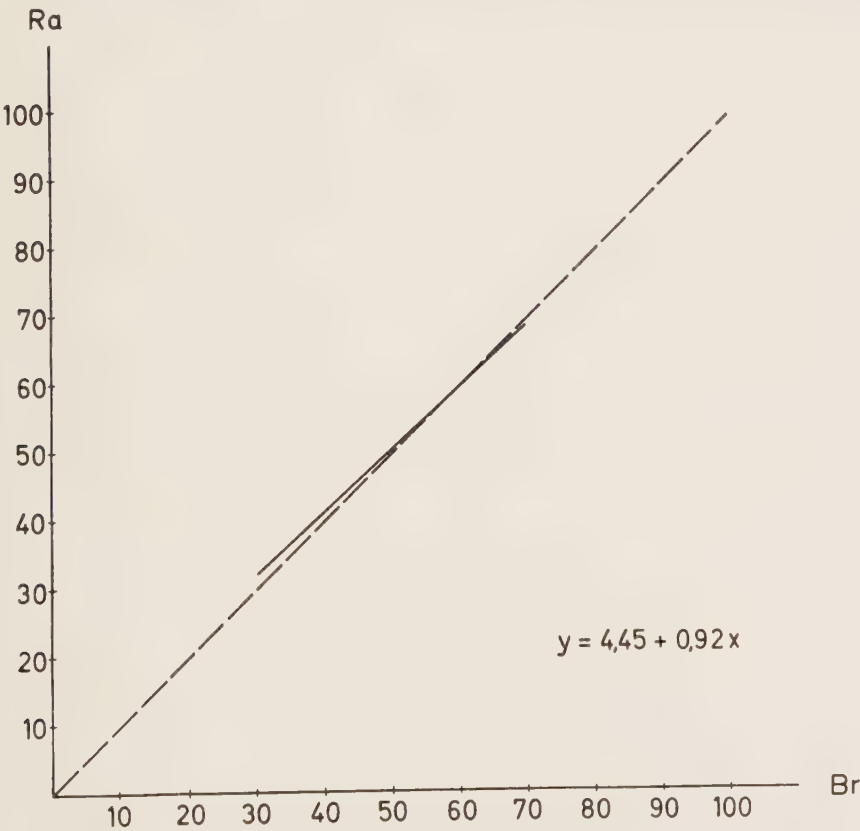


Fig. 21.
Distribution of perfusion in 29 cases. The regression line estimated from the results in 29 of the cases presented in Figure 16. Cases with the perfusion of the right lung <30 per cent or >70 per cent of the perfusion of both lungs (estimated with bronchosprometry) were excluded from this calculation.

wash-in time the patient was asked to take some deep breaths repeatedly during the wash-in procedure. This might cause a discrepancy with bronchspirometry where deep breathing was not encouraged, as in some pathological cases bronchi which are closed during normal breathing, open for air passage at maximal inspiration, and consequently allow wash-in of Xe-133 in parts of the lungs that have not taken part in the nitrogen wash-out during bronchspirometry.

Bronchspirometric determination of the distribution of perfusion is based on the oxygen uptake of each lung. Only perfusion of alveoli in open connection with the main bronchus and the tube can thus be registered, and the perfusion of hypoventilated alveoli can be correctly appreciated only if the alveolar oxygen content is sufficient for the blood to be saturated during the passage through the alveolar capillaries. In order to lessen the effect of regional hypoventilation on the determination of perfusion, the oxygen content of the spirometer gas was kept at about 35 per cent. Still, the fact remains that the perfusion of the lung parenchyma behind a severe bronchial stenosis cannot be accurately judged by bronchspirometry.

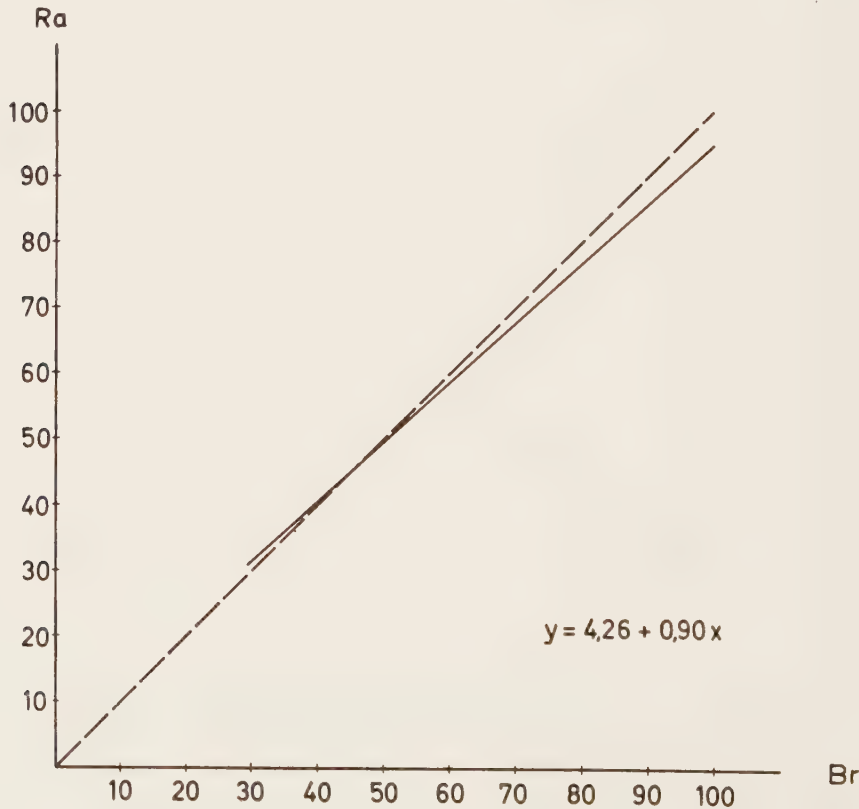


Fig. 22.
Distribution of ventilation in 35 cases. The regression line estimated from the results of the cases presented in Figure 17.

With radiospirometry, the perfusion is registered independently of the ventilation as long as there is gas in the alveoli. The perfusion of atelectatic parts may sometimes be registered as a sharp peak similar to the peak caused by the passage of xenon through the heart and vessels. Such a peak coincides in time with the ascending part of the record line. The points 1 and 2 in Figure 16 represent cases exemplifying this discrepancy between the two methods. The patient who is represented by point 1 had little or no ventilation in his diseased lung according to bronchspirometry and radiospirometry, and, consequently, the perfusion through the lung could not be judged bronchspirometrically. With radiospirometry 20 per cent of the perfusion was found to go through the apical field of the diseased lung. Angiopneumography verified the presence of blood flow within the apical lung field. The patient, who is represented by point 2 in Figure 16, had 15 per cent of his ventilation in the diseased lung according to the bronchspirometry, which makes it probable that the perfusion of the diseased lung was underestimated by bronchspirometry. Presumably this mechanism is responsible for the discrepancy between bron-

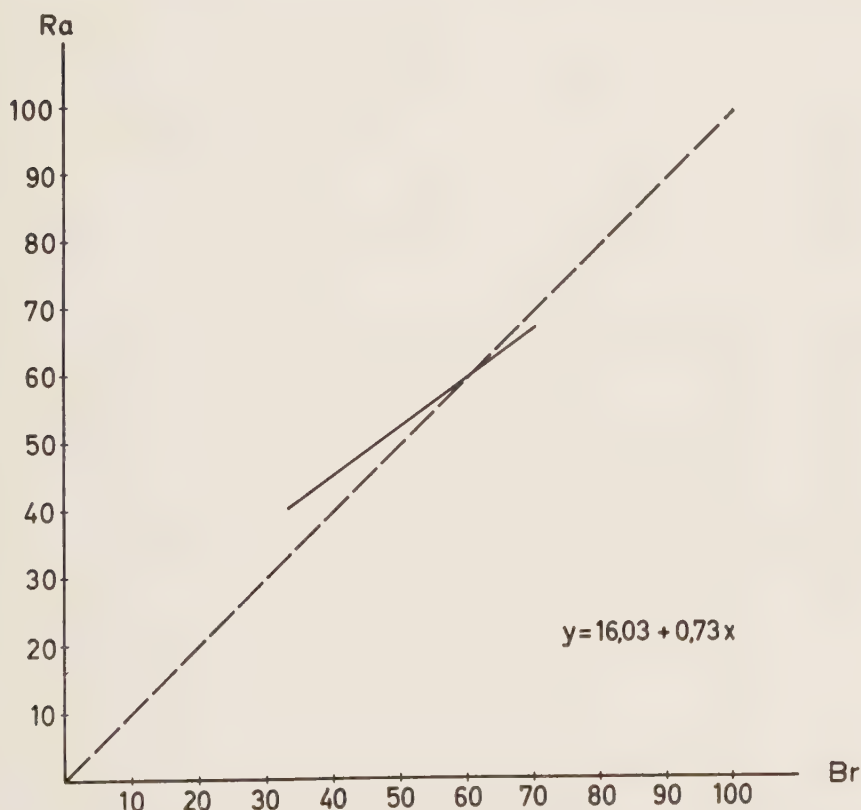


Fig. 23.
Distribution of functional residual capacity in 21 cases. The regression line estimated from the results of the cases presented in Figure 18.

chospirometry and radiospirometry as regards perfusion. The existence of arterial hypoxemia during bronchospirometry would support this assumption, but blood gas analyses during bronchospirometry have not been performed in this series.

Several different factors may explain the discrepancy between the bronchospirometric and radiospirometric results. For radiospirometry: the radioactivity in different parts of the lungs is not recorded with equal sensitivity, Compton scatter and chest wall radiation influence the counting rates. For bronchospirometry: the perfusion in poorly ventilated parts of the lung may be underestimated. With this in mind, it is astonishing that the agreement between the methods is so great. The results of this investigation are regarded as supporting the hypothesis that radiospirometry yields information on the distribution of perfusion, ventilation, functional residual capacity and vital capacity, which for clinical use is equivalent to that obtained from bronchospirometry. The discrepancies discussed above should be considered when judging the radiospirometric results, especially in estimates of FRC.

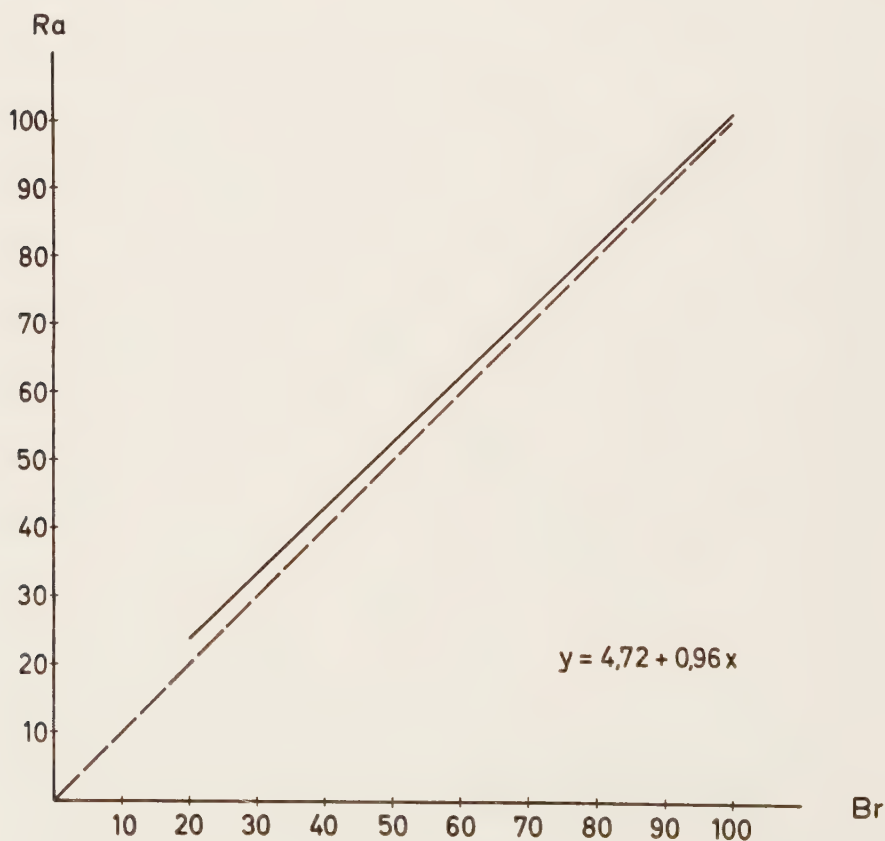


Fig. 24. Distribution of vital capacity in 29 cases. The regression line estimated from the results of the cases presented in Figure 19.

Chapter V

RADIOSPIROMETRY IN NORMAL SUBJECTS

Since it had turned out that radiospirometry in patients with lung diseases gave information essentially equivalent to that obtained by bronchospirrometry, it seemed justifiable to use radiospirometry in clinical routine work. In order to make it possible to judge the results properly, the variations in radiospirometric results in normal subjects had to be settled.

MATERIAL

Thirty-eight volunteers were studied, representing three groups:

Group	Number of subjects	Sex	Mean age	Age range
I	15	female	22	18—31
II	12	male	20	19—27
III	11	male	44	38—49

The criteria for normality were:

(1) No history and no clinical signs of lung disease or heart disease. In group III only non-smokers were accepted, because smokers at that age often have developed chronic bronchitis, the symptoms of which may be overlooked.

(2) Normal chest X-ray. All volunteers were also subjected to spirometry. The following parameters were estimated: VC, FRC, FEV_{1.0} and lung clearance index (Becklake 1952; Bouhuys, Hagstam & Lundin 1955). Normal values according to Grimby and Söderholm (1963) (VC and FRC), Berglund, Birath, Bjure, Grimby, Kjellmer, Sandqvist and Söderholm (1963) (FEV_{1.0}) and Svanberg (1957) (lung clearance index) were found in all subjects, except two in group I, whose VC was slightly (0.2 L) below the lower normal limit.

METHODS

Radiospirometry was performed with the technique described in Chapter III, page 36. In most cases, duplicate determinations were made of the distribution of perfusion and ventilation. Only the first of these determinations was used for calculation of

the normal values in Tables 5—11. The second determination was used for studies on the methodological error (Chapter VI, p. 62). In view of the time needed for the rebreathing procedure, duplicate determinations of lung volumes were not performed.

RESULTS

The distribution of perfusion, ventilation, functional residual capacity and vital capacity in the three groups is presented in Tables 5—8. As already pointed out, the figures for the individual fields can hardly be exploited in clinical routine as they vary too much due to individual differences regarding the shape of the chest. The most relevant data in the tables are:

<i>Q R</i>	<i>Q Ra</i>	<i>Q Rb</i>	
<i>V R</i>	<i>V Ra</i>	<i>V Rb</i>	ind. <i>Q I</i> — <i>IV</i>
<i>FRC R</i>	<i>FRC Ra</i>	<i>FRC Rb</i>	ind. <i>V I</i> — <i>IV</i>
<i>VC R</i>	<i>VC Ra</i>	<i>VC Rb</i>	<i>V/Q I</i> — <i>IV</i>

These parameters in the three groups were subjected to statistical analysis. The hypothesis that the mean values were equal in all three groups was tested. The test was made as a variance analysis (See Statistical Methods, p. 6). It turned out that there was no significant difference between the groups. The relations between regional perfusion, ventilation and functional residual capacity in the different fields, expressed as ind. *Q*, ind. *V* and *V/Q* are presented in Tables 9—11. The results were subjected to the same statistical analysis as the parameters above. No significant difference between the groups was found.

As there was no difference in the radiospirometric results between a group of young men and a group of middle-aged men, it was judged as biologically improbable that different results would be obtained in a fourth group of middle-aged women. It was thus decided not to include such a group in the material.

It was also possible to pool the results of the three groups in order to make them easier of survey. Before the figures (*Q R*, *V R*, *FRC R* and *VC R*) were further treated, their adaptation to the normal distribution was tested by plotting on Normal-probability Paper. The adaptation to the normal distribution was found to be good. Consequently, the tolerance intervals for the different parameters could be estimated (Table 12). With confidence 95 per cent the interval will contain 95 per cent of a normal population.

DISCUSSION

The function of the right lung was found to be about 53 per cent of the total function, which agrees surprisingly well with earlier results of bronchspirometry in

Table 5

DISTRIBUTION OF PERFUSION (Q)

RIGHT LUNG					LEFT LUNG				
	Q II	Q IV	Q R	Q I	Q III	Q L	Q Ra	Q Rb	
Mean	Group I	21.8	30.7	52.4	20.1	27.5	47.6	52.2	52.8
	" II	23.1	29.1	52.2	21.8	26.0	47.8	51.6	52.8
	" III	22.7	30.6	53.4	19.9	26.8	46.6	53.4	53.4
	Total material	—	—	52.6	—	—	—	52.4	52.9
SD	Group I	3.3	3.0	2.3	2.6	3.0	2.3	3.0	2.4
	" II	2.2	3.1	2.4	3.4	2.5	2.4	3.4	2.5
	" III	3.7	3.8	1.8	3.6	3.5	1.8	3.1	1.8
	Total material	—	—	2.2	—	—	—	3.2	2.2
Range	Group I	17.1—27.4	23.9—34.9	47.9—55.9	15.4—24.7	23.7—33.8	44.1—52.1	47.2—58.2	47.2—56.1
	" II	19.4—27.1	23.0—33.0	48.3—56.6	18.4—30.0	19.9—29.8	43.4—51.7	47.3—55.9	49.3—57.2
	" III	16.7—28.9	24.0—36.6	50.1—55.9	14.1—25.7	21.4—31.9	44.1—49.9	48.1—58.5	50.8—55.9
	Total material	—	—	47.9—56.6	—	—	—	47.2—58.5	47.2—57.2

Group I: 15 women aged 18—31 years
 " II: 12 men aged 19—27 years
 " III: 11 men aged 38—49 years
 Total material: Group I, II and III

DISTRIBUTION OF VENTILATION (V)

RIGHT LUNG				LEFT LUNG				
	VII	VIV	VR	VI	VIII	VL	VRa	VRb
Group I	21.5	30.3	51.9	21.4	26.7	48.1	50.0	53.4
“ II	22.9	30.0	52.8	22.6	24.7	47.2	50.8	54.7
“ III	21.3	31.8	53.1	20.6	26.3	46.9	50.9	54.8
Total material	—	—	52.5	—	—	—	50.5	54.2
Group I	3.9	3.2	2.7	3.3	4.6	2.7	3.0	3.8
“ II	1.6	3.4	2.9	3.3	3.0	2.9	2.8	4.4
“ III	3.4	4.0	1.9	3.9	3.5	1.9	2.7	2.5
Total material	—	—	2.6	—	—	—	2.8	3.6
Group I	15.2—29.0	25.9—36.1	48.5—55.9	13.9—26.0	20.2—37.5	44.1—51.5	45.4—55.7	47.1—58.3
“ II	20.8—26.4	22.1—33.1	46.8—55.2	17.8—29.0	19.6—29.1	44.8—53.2	46.1—55.0	45.8—60.3
“ III	17.2—27.7	25.8—37.6	49.2—55.8	15.7—27.5	19.0—30.9	44.2—50.8	45.6—54.8	51.9—59.7
Total material	—	—	46.8—55.9	—	—	—	45.4—55.7	45.8—60.3

Table 7

DISTRIBUTION OF FUNCTIONAL RESIDUAL CAPACITY (FRC)

		RIGHT LUNG				LEFT LUNG			
		FRC II	FRC IV	FRC R	FRC I	FRC III	FRC L	FRC Ra	FRC Rb
Mean	Group I	22.4	31.4	53.8	20.7	25.4	46.2	52.1	55.3
	" II	24.3	30.7	55.0	21.5	23.5	45.0	53.1	56.7
	" III	22.8	33.2	56.0	19.4	24.5	44.0	54.0	57.5
	Total material	—	—	54.8	—	—	—	52.9	56.4
SD	Group I	2.7	3.0	2.8	3.2	3.6	2.8	3.1	3.5
	" II	1.8	2.4	1.7	2.0	2.2	1.7	1.9	2.8
	" III	3.3	3.7	2.5	3.1	3.0	2.5	2.8	2.6
	Total material	—	—	2.5	—	—	—	2.8	3.1
Range	Group I	15.3—26.2	25.7—36.2	48.7—59.0	13.7—25.8	20.6—36.0	41.0—51.3	46.1—57.3	49.3—62.0
	" II	22.2—27.6	25.7—33.6	52.1—57.2	19.0—27.0	19.7—28.9	42.8—47.9	50.5—55.7	49.7—59.5
	" III	17.0—29.3	28.0—38.1	51.9—59.5	15.6—24.4	19.3—31.2	40.5—48.1	48.1—56.8	53.6—61.6
	Total material	—	—	48.7—59.5	—	—	—	46.1—57.3	49.3—62.0

Table 9

PERFUSION INDEX (ind. Q)

		RIGHT LUNG			LEFT LUNG		
		ind. Q II	ind. Q IV	ind. Q R	ind. Q I	ind. Q III	ind. Q L
Mean	Group I	0.97	0.98	0.98	0.98	1.09	1.03
	„ II	0.95	0.95	0.95	1.01	1.11	1.06
	„ III	1.00	0.92	0.95	1.02	1.09	1.06
	Total material	0.97	0.95	0.96	1.00	1.10	1.05
SD	Group I	0.10	0.07	0.05	0.13	0.09	0.06
	„ II	0.07	0.05	0.04	0.09	0.09	0.05
	„ III	0.07	0.05	0.03	0.11	0.11	0.04
	Total material	0.08	0.06	0.04	0.11	0.10	0.05
Range	Group I	0.76—1.12	0.85—1.09	0.91—1.06	0.85—1.34	0.94—1.27	0.93—1.13
	„ II	0.86—1.07	0.87—1.02	0.86—0.99	0.86—1.14	0.95—1.27	1.01—1.18
	„ III	0.88—1.12	0.82—1.01	0.92—1.02	0.82—1.15	0.98—1.30	0.98—1.11
	Total material	0.76—1.12	0.82—1.09	0.86—1.06	0.82—1.34	0.94—1.30	0.93—1.18

Table 10

VENTILATION INDEX (ind. V)

		RIGHT LUNG			LEFT LUNG		
		ind. V II	ind. V IV	ind. V R	ind. V I	ind. V III	ind. V L
Mean	Group I	0.96	0.97	0.97	1.04	1.05	1.04
	„ II	0.94	0.97	0.96	1.05	1.05	1.05
	„ III	0.94	0.96	0.95	1.06	1.07	1.07
	Total material	0.95	0.97	0.96	1.05	1.06	1.05
SD	Group I	0.11	0.04	0.05	0.09	0.13	0.06
	„ II	0.03	0.07	0.04	0.10	0.11	0.05
	„ III	0.08	0.07	0.04	0.12	0.11	0.06
	Total material	0.08	0.06	0.04	0.10	0.11	0.06
Range	Group I	0.73—1.18	0.92—1.08	0.88—1.04	0.91—1.27	0.76—1.30	0.95—1.15
	„ II	0.90—1.01	0.85—1.11	0.88—1.02	0.88—1.17	0.87—1.22	0.97—1.14
	„ III	0.86—1.14	0.89—1.12	0.88—1.01	0.84—1.19	0.88—1.20	0.99—1.16
	Total material	0.73—1.18	0.85—1.12	0.88—1.04	0.84—1.27	0.76—1.30	0.95—1.16

Table 11

VENTILATION/PERFUSION RATIO (V/Q)

		RIGHT LUNG			LEFT LUNG		
		V/Q II	V/Q IV	V/Q R	V/Q I	V/Q III	V/Q L
Mean	Group I	0.99	0.99	0.99	1.07	0.96	1.01
	„ II	1.00	1.03	1.01	1.04	0.95	0.99
	„ III	0.94	1.04	0.99	1.05	0.99	1.01
	Total material	0.98	1.02	1.00	1.05	0.97	1.00
SD	Group I	0.07	0.08	0.03	0.11	0.08	0.04
	„ II	0.09	0.06	0.04	0.11	0.13	0.05
	„ III	0.07	0.07	0.05	0.16	0.10	0.06
	Total material	0.08	0.07	0.04	0.12	0.10	0.05
Range	Group I	0.86—1.12	0.84—1.11	0.95—1.04	0.75—1.22	0.81—1.11	0.94—1.05
	„ II	0.89—1.16	0.97—1.16	0.94—1.08	0.85—1.22	0.77—1.21	0.92—1.07
	„ III	0.81—1.03	0.91—1.14	0.91—1.07	0.79—1.32	0.86—1.18	0.93—1.12
	Total material	0.81—1.16	0.84—1.16	0.91—1.08	0.75—1.32	0.77—1.21	0.92—1.12

Table 12

Confidence intervals

With confidence 95 per cent the interval will contain 95 per cent of a normal population.

Right lung:

Q R	52.6±5.4	(47.2; 58.0)
V R	52.5±6.4	(46.1; 58.9)
FRC R	54.8±6.2	(48.6; 61.0)
VC R	52.0±5.2	(46.8; 57.2)

Indices:

ind. Q R	0.96±0.10	(0.86; 1.06)
ind. V R	0.96±0.10	(0.86; 1.06)
V/Q R	1.00±0.10	(0.90; 1.10)
ind. Q L	1.05±0.12	(0.93; 1.17)
ind. V L	1.05±0.15	(0.90; 1.20)
V/Q L	1.00±0.12	(0.88; 1.12)

Right apical field:

Q Ra	52.4±7.9	(44.5; 60.3)
V Ra	50.5±6.9	(43.6; 57.4)
FRC Ra	52.9±6.9	(46.0; 59.8)
VC Ra	49.9±6.6	(43.3; 56.5)

ind. Q I	1.00±0.27	(0.73; 1.27)
ind. V I	1.05±0.25	(0.80; 1.30)
V/Q I	1.05±0.30	(0.75; 1.35)
ind. Q II	0.97±0.20	(0.77; 1.17)
ind. V II	0.95±0.20	(0.75; 1.15)
V/Q II	0.98±0.20	(0.78; 1.18)

Right basal field:

Q Rb	52.9±5.4	(47.5; 58.3)
V Rb	54.2±8.9	(45.3; 63.1)
FRC Rb	56.4±7.6	(48.8; 64.0)
VC Rb	53.7±7.4	(46.3; 61.1)

ind. Q III	1.10±0.25	(0.85; 1.35)
ind. V III	1.06±0.27	(0.79; 1.33)
V/Q III	0.97±0.25	(0.72; 1.22)
ind. Q IV	0.95±0.15	(0.80; 1.10)
ind. V IV	0.97±0.15	(0.82; 1.12)
V/Q IV	1.02±0.17	(0.85; 1.19)

normal subjects (Table 2). Also the standard deviations were approximately equal with radiospirometry and bronchospirrometry. In the present material, the FRC of the right lung was relatively greater than the perfusion and ventilation in spite of the fact that the difference in FRC between the lungs may be slightly underestimated by the present technique, due to xenon in the heart and chest wall. As a result of the relatively larger FRC of the right lung, the mean perfusion index (ind. Q) and the mean ventilation index (ind. V) were slightly below 1 for the right lung, and slightly above 1 for the left lung. The ventilation/perfusion ratio (V/Q) was, on the other hand, close to 1 for both lungs. This indicates that the ventilation and perfusion per unit lung volume were somewhat lower in the right lung. It is interesting to note that Svanberg (1957), on analysis of the nitrogen wash-out during bronchospirrometry, found that the alveolar air dilution per breath was somewhat larger in the left lung than in the right one, both in the sitting and in the supine positions. This must be interpreted as the ventilation per unit volume being somewhat lower in the right lung than in the left one, if there is no reason to believe that the distribution of inspired gas should be more uneven in the right lung in normal man.

Chapter VI

REPRODUCIBILITY OF THE RADIOSPIROMETRIC RESULTS

Duplicate determinations of two different types were carried out:

(1) Duplicate determinations of the distribution of perfusion and ventilation during the same investigation.

(2) Two complete investigations at several days' interval with determination of the distribution of perfusion, ventilation, functional residual capacity and vital capacity.

MATERIAL

Duplicate determinations (1) of the perfusion were carried out in 33 normal subjects and in 31 patients with lung disease. Duplicate determinations of the ventilation were carried out in 31 normal subjects and in 36 patients with lung disease.

Two complete investigations (2) were performed in 13 normal subjects. If duplicate determinations of perfusion or ventilation were made at any of these investigations, only the result of the first determination was used for calculating the differences between the two investigations.

RESULTS

In the comparison between duplicate determinations (1), the following parameters were studied: $Q R$, $Q R a$, $Q R b$, $V R$, $V R a$ and $V R b$. The results, expressed as mean differences and errors of a single determination, are presented in Table 13.

If a single determination gives $Q R$ or $V R = X$, the true value was calculated to be within the following limits in 95 per cent of the determinations:

at determination of perfusion in normal subjects: $X \pm 1.0$

„ „ „ „ in patients with lung disease: $X \pm 2.9$

at determination of ventilation in normal subjects: $X \pm 2.7$

„ „ „ „ in patients with lung disease: $X \pm 3.5$

In the comparison between two complete investigations (2), $FRC R$, $FRC R a$, $FRC R b$, $VC R$, $VC R a$ and $VC R b$ were studied in addition to the above mentioned parameters. The results are summarized in Table 13. When the differences between

Table 13

Methodological errors in radiospirometry.

	Duplicate determinations during one investigation				Two investigations on different days	
	Normal subjects *)		Patients with lung disease **)		13 normal subjects	
	mean diff.	e	mean diff.	e	mean diff.	e
<i>Q R</i>	+ 0.1	0.8	+ 0.1	1.0	— 0.2	1.4
<i>Q Ra</i>	+ 0.2	1.3	+ 0.3	1.8	— 1.7	2.8
<i>Q Rb</i>	0.0	1.0	+ 0.1	1.3	+ 0.9	1.4
<i>V R</i>	+ 0.2	1.3	+ 0.5	1.7	+ 0.2	1.0
<i>V Ra</i>	+ 0.7	1.7	+ 0.5	2.5	— 0.1	1.9
<i>V Rb</i>	— 0.1	2.0	+ 0.4	2.6	+ 0.3	1.6
<i>FRC R</i>					— 0.1	1.1
<i>FRC Ra</i>					— 0.2	1.4
<i>FRC Rb</i>					— 0.1	1.4
<i>VC R</i>					— 0.5	1.4
<i>VC Ra</i>					+ 0.4	2.5
<i>VC Rb</i>					— 1.3	2.6

*) 33 Subjects in the perfusion study and 31 in the ventilation study.

**) 31 Subjects in the perfusion study and 36 in the ventilation study.

duplicate determinations during the same investigation, and the differences between two investigations were compared (F-test) the differences between the two investigations proved to be significantly larger for *Q R* (*) and *Q Ra* (**). As regards *Q Rb* and ventilation (*V R*, *V Ra* and *V Rb*) there were, however, no significant differences.

DISCUSSION

The differences between duplicate determinations during the same investigation may be due to random error in the recording of the counting rate, to variations in the distribution of function, and to changes in the subject's position in relation to the counters.

It would be possible to make duplicate determinations of the distribution of perfusion and ventilation during routine radiospirometries. Duplicate determinations should, however, be recommended only if the random error of a single determination is large enough to be of importance. This analysis of duplicate determinations was performed in order to establish the influence of the random error. As expected, the random error was smaller for normal subjects than for patients with lung disease. Even in such patients, the true value ought not to be more than 3.5 per cent above or below the value for the relative function of the right lung found by a single determination. This inaccuracy was not considered large enough to justify duplicate determinations in the routine work.

Due to the time necessary for the rebreathing procedure, and for the radioactivity to disappear after the procedure, duplicate determinations of the lung volumes during the same investigation were not performed.

Differences between examinations made on different days may be due to the same mechanisms, which were supposed to cause differences between duplicate determinations during the same investigation, but also to different positioning in relation to the counters. This may explain why the differences were larger than between duplicate determinations (1) for perfusion.

The reproducibility was found to be nearly equal for perfusion, ventilation, functional residual capacity and vital capacity in normal subjects.

Investigations on different days in patients with lung disease were not included in the methodological study, as the distribution of function in such patients may be subjected to large variations within a short time, due to the disease.

Chapter VII

ESTIMATION OF THE DISTRIBUTION OF PERFUSION DURING MAINTAINED NORMAL BREATHING

The estimation of regional perfusion during breath-holding has some disadvantages. Active cooperation from the subject is required, and it is sometimes difficult for the subject to maintain ambient pressure in the chest during breath-holding.

When estimating perfusion during normal breathing (Heckscher et al. 1966), the regional perfusion is represented by the highest point of the record line. Theoretically, the estimation of the perfusion during normal breathing might be less reliable for the following reasons:

(1) The peak representing regional perfusion might be subjected to greater random error than the plateau recorded during breath-holding.

(2) The perfusion within poorly *ventilated* regions might be overestimated compared to the perfusion within well ventilated regions, as the wash-out of Xe-133 starts at the moment when the first xenon enters the alveolar air, and, thus, before the maximal concentration has been reached.

(3) The perfusion within poorly *perfused* regions might be overestimated compared to the perfusion within well perfused regions, as dead space air containing Xe-133 might be inhaled in poorly perfused regions before the peak of radioactivity has been reached (Fig. 13).

In order to evaluate the practical importance of these theoretical considerations, the distribution of perfusion was estimated both during breath-holding and during normal breathing in a number of healthy volunteers and patients with lung disease.

Ad. 1. The random error when estimating regional perfusion during normal breathing, as judged from duplicate determinations, was studied in 8 healthy volunteers and in 17 patients with lung disease. The results are presented in Table 14 together with corresponding figures from determinations during breath-holding.

Ad. 2 and 3. These mechanisms both tend to overestimate the relative perfusion of a poorly functioning lung during normal breathing, as compared to breath-holding. To get information about the practical importance of these theoretical sources of error when determining perfusion during normal breathing, estimations were performed, both during breath-holding and during normal breathing, in three groups of subjects, presented in Table 15.

In order to facilitate this comparison, the results were expressed as the perfusion of the best lung in per cent of the total perfusion. In normal subjects (Group I),

Table 14

The random errors as judged from duplicate determination of the relative perfusion of the right lung ($Q R$) during breath-holding and during normal breathing.

Subjects	Number of subjects	Error of a single determination	
		Breath-holding	Normal breathing
Healthy volunteers	33 8	0.8	0.9
Patients with lung disease	31 17	1.0	1.5

Table 15

The relative perfusion of the best lung as estimated during breath-holding and during normal breathing.

Group I: Healthy volunteers.

Group II: Patients with a perfusion or ventilation of the best lung of less than 63 per cent of total.

Group III: Patients with a perfusion or ventilation of the best lung of more than 63 per cent of total.

		Relative perfusion of the best lung			
		Breath-holding		Normal breathing	
		Mean	SD	Mean	SD
I	12	53.4	1.7	52.5	1.6
II	22	55.3	—	54.7	—
III	11	70.5	—	67.7	—

as well as in patients with moderate abnormalities of the distribution of perfusion (Group II: the function of the best lung < 63 per cent of total), there were no significant differences between the results obtained during breath-holding and during normal breathing. In Group III (patients with the perfusion or the ventilation of the best lung > 63 per cent of total) the perfusion of the best lung was on an average 70.5 per cent, when estimated during breath-holding, and 67.7 per cent when estimated during normal breathing. In all cases but one, the relative perfusion of the best lung was greater during breath-holding. The individual results are presented in Table 16.

Conclusions

The random error was slightly greater when estimating perfusion during normal breathing, as compared to breath-holding, but yet it was judged to be acceptable for clinical routine work.

Table 16

The relative perfusion and ventilation of the best lung in group III (Table 15).

Case	Perfusion of the best lung (<i>QR</i> or <i>QL</i>)			Ventilation of the best lung (<i>VR</i> or <i>VL</i>)
	Breath-holding	Normal breathing	Difference	
E.A.	90.0	87.6	— 2.4	88.7
R.O.	80.6	76.2	— 4.4	76.6
E.L.	75.7	71.6	— 4.1	79.2
J.J.	74.2	72.6	— 1.6	76.6
M.N.	68.9	63.6	— 5.3	74.6
A.N.	67.8	68.8	+ 1.0	61.9
O.A.	67.2	63.0	— 4.2	61.0
J.N.	64.6	62.0	— 2.6	61.6
G.L.	63.5	63.2	— 0.3	73.2
J.O.	61.3	57.0	— 4.3	63.3
O.E.	61.2	59.1	— 2.1	70.8

In normal subjects, and in patients with small differences in function, both methods gave almost identical results.

In all but one of the cases in the group with greater functional differences between the lungs, the relative perfusion of the best lung was smaller when estimated during normal breathing. The result supports the theoretical assumption that estimation of perfusion during maintained breathing would tend to overestimate the function of a poorly functioning lung. The differences in this material, however, were relatively small. This tendency to overestimate the function of a poorly perfused and/or badly ventilated lung should be taken into consideration when the results of estimation of perfusion during maintained breathing are evaluated.

For most routine purposes it should be possible to estimate the distribution of perfusion during normal breathing.

Chapter VIII

GENERAL DISCUSSION

The purpose of this study was to work out a method using radioisotopes and external counters for estimation of regional lung function, which could replace bronchspirometry in clinical routine. The apparatus and the technique described in Chapter III were developed for this purpose.

Comparison between bronchspirometry and radiospirometry.

Considering the very different principles which radiospirometry and bronchspirometry have, it is surprising that the results of radiospirometry and bronchspirometry agreed so well. It was especially surprising in regard to the vital capacity, since changes in the geometry of the counting fields could be expected during this part of the procedure.

As can be seen from the regression lines (Figs. 20—24), there was a general tendency towards overestimating the function of the diseased lung with radiospirometry compared to bronchspirometry. For those procedures having short duration (perfusion, ventilation and vital capacity) the overestimation was of the same magnitude as the scatter radiation from the xenon-free lung at unilateral inhalation of Xe-133 (p. 31). This radiation was assumed to be due to Compton scatter and gave counting rates of less than 5 per cent for perfusion and ventilation of a xenon-free lung. During the rebreathing procedure there was Xe-133 in the extrapulmonary tissue also, and this tended to further overestimate the volume of the diseased lung. By extrapolation of the regression line in Figure 23, the counting rate after 5 minutes' rebreathing recorded from a non-functioning lung was estimated to be 16 per cent of the counting rate recorded from the other side.

A correction factor for the different phases of the investigation might be calculated on the basis of the regression lines. It was, however, for clinical purposes not considered necessary to complicate the calculations further. The more even the distribution of function is, the less the importance of the Compton scatter and the radiation from the chest wall. These phenomena should be of practical significance for the evaluation of the results only in cases where there are large regional differences in function. The differences mentioned above should nevertheless be kept in mind when evaluating the radiospirometric results.

There was also good agreement between the mean values for the normal subjects in this radiospirometric study and the mean values for bronchospirometric investigation of normal subjects as given by Svanberg (1957) and Arborelius (1966) (Table 2, p. 10). For this reason, it was not thought necessary to have a greater number of normal subjects than were used, even if that had not met with difficulties, the investigation not being uncomfortable for the subject. The observation that the ventilation per unit of lung volume was found to be larger in the left lung than in the right one both with radiospirometry and bronchospirometry, illustrates the good agreement between these two methods.

Errors in the methods: The intubation procedure during bronchospirometry should tend to reduce the dependability of the method, as, among other things, random variations in the distribution of ventilation as a result of the accumulation of mucus tend to arise in anaesthetized bronchi. On the other hand, random variations during radiospirometry could be caused by changes in the subject's position in relation to the counters during the investigation. An attempt has been made to reduce this latter source of error by putting in spot-lights (p. 28). The different results obtained from investigations performed on two different days could depend on the counting fields' being marked differently on the two separate occasions. The results of the duplicate determinations of perfusion during one investigation, as compared to determinations during investigations on two different days, indicate that this mechanism might be of importance. The reproducibility of radiospirometry was nevertheless found to be better than that of bronchospirometry both with duplicate determinations in the same investigation, and in investigations on two different days.

Limitations in the use of bronchospirometry and radiospirometry

In some cases it may not be possible to perform bronchospirometry, or the results may not be reliable. For anatomical reasons, it is not possible to perform bronchospirometry in children, even if a small double lumen catheter is used, as there is too great airway resistance. Intubation of patients with deformed trachea and bronchi may be very difficult, and, sometimes, impossible to carry out. In other cases topographical abnormalities might cause mis-interpretation of the results, even if the intubation is successful. Furthermore, the bronchospirometric examination is tiresome for patients in bad physical condition.

However, radiospirometry has its limitations, also. In patients with pronounced chest deformities, the relative function of each lung cannot be evaluated by the routine proceedings used in this study. Dislocation of the mediastinum might be a cause for mis-interpreting the results. Such dislocations will, as a rule, be discovered by the fluoroscopic examination.

The exposure to radiation during radiospirometry is considerably less than the maximal weekly amount established for radiological personnel, and as radiospiro-

metry is, besides, not troublesome to the patient, it can be repeatedly performed in the same subject, when this is clinically indicated. For practical reasons, this has not been possible to the same extent with bronchospirometry.

The relationships between perfusion, ventilation and FRC within each counting field, expressed as ind. Q, ind. V and V/Q, have been calculated in order to facilitate the clinical evaluation of the results. Since these indices are calculated from data expressed in per cent of the total function, abnormal relation within one counting field may, for mathematical reasons, lead to the V/Q ratios becoming abnormal within other fields.

The logic in this is illustrated thus: A normal subject is assumed to have an alveolar ventilation of 4 litres. The radiospirometric measurements of the ventilation are influenced by xenon in alveoli as well as in airways within the counting fields. The ventilation, measured radiospirometrically, is assumed to be approximately 6 L/min., and the cardiac output to be 5 L/min. Both ventilation and perfusion are assumed to be the same in both lungs (Column I in Table 17).

Table 17

The influence of a local reduction of blood flow on V/Q.

	I		II	
	Right lung	Left lung	Right lung	Left lung
Ventilation (L/min.)	3	3	5.4	5.4
Ventilation in per cent of total (V R and V L, respectively)	50	50	50	50
Perfusion (L/min.)	2.5	2.5	4.5	0.5
Perfusion in per cent of total (Q R and Q L, respectively)	50	50	90	10
V/Q ratio (calculated from the absolute values)	1.2	1.2	1.2	10.8
V/Q ratio (calculated from percental values)	1.0	1.0	0.56	5.0

In Column II the left lung is thought to be affected by a pathological process, which reduces its perfusion to 0.5 L/min. The cardiac output can be assumed to remain unchanged, but the major part passes through the right lung. The ventilation will increase in order to oxygenate this larger amount of blood, and adequately remove carbon dioxide from it. The total ventilation must be larger than for the normal lungs, as most of the left lung's ventilation goes to unperfused alveoli and is, thus, dead space ventilation. The relation between ventilation and perfusion in the right lung expressed in litres per minute should remain unchanged: 1.2, but the relation between the percentage values is 0.56, which is outside normal range. Abnormal ventilation-perfusion ratios for the left lung have thus caused abnormal V/Q for the

right lung, despite the fact that the right lung's actual ventilation-perfusion ratio should be unchanged. This example was chosen to show a nearly maximal effect on the indices of the normal lung. In most cases the pathological process will affect both perfusion and ventilation either primarily or due to functional adaptation (Arborelius 1966) which would decrease the error in V/Q ratio mentioned above. When clinically evaluating V/Q ratios, it must be remembered that if the relations between ventilation, perfusion and volume within one part of the lung are abnormal, the V/Q ratios for other counting fields must be judged with care. It should also be noted that, due to accumulation of Xe-133 in the chest wall during the rebreathing period, radio-spirometry will overestimate the FRC of a poorly functioning lung, thus artificially decreasing ind. Q and ind. V for that lung.

*Can radiospirometry give more information than can be obtained
with bronchosprometry?*

With bronchosprometry in the supine position, a functional defect influences the results equally, wherever it may be located in the lung (the influence of the pressure differences in dorso-ventral direction being neglected). It can be calculated mathematically how much the loss of a known volume of functioning lung tissue will influence the distribution of function. Arborelius and Miörner (1967) developed this from the basis that the lungs have 19 segments, the left lung 9 and the right lung 10. As these segments are not of the same size, the expression "functional unit" was preferred, each corresponding in size to an average segment. The right lung's function should theoretically be 52.6 per cent, which happens to be identical with the value for perfusion of the right lung in the present normal material. The decrease of the function of each lung, expressed as per cent of the total function, was calculated for the loss of 1 to 10 "functional units" (Table 18). The loss of one "functional unit" in the right lung decreases the function from the average normal 52.6 per cent to 50.0 per cent, *i.e.* 2.6 per cent. The decrease becomes numerically greater with the loss of every additional "functional unit", and the last "functional unit" represents 10 per cent. As judged from the bronchosprometric values in Arborelius' 24 normal subjects, a subject who normally has 53.5 per cent of the total perfusion in the right lung, must thus lose the perfusion corresponding to 3 "functional units" (= 8.8 per cent) before the bronchosprometric values will fall outside the normal range (53.5 ± 2.5 SD).

With radiospirometry, a functional defect also influences the results equally, wherever it may be located in the lung, provided the radioactivity in all parts of the lungs is recorded with equal detector sensitivity. In the technique used, this may apply for most of the lung tissue. The influence of a functional loss in the borderline area between the apical and the basal field is, however, somewhat less than that of a functional loss in the centre of a counting field, as shown in the experiment

with the lung model (p. 33). The latero-basal parts of the lungs also fall outside the area having high detector sensitivity. Judged from the good agreement between the results of bronchspirometry and radiospirometry in normal subjects, as well as in patients with lung disease, the practical importance of these differences in sensitivity seems to be small. The confidence interval calculated from the results of radio-

Table 18

The influence of the loss of one to ten "functional units"
expressed in per cent of total on right (R) and left (L) side.
N.V. = numerical value of unit.

N.V.	R	Units lost	L	N.V.
	52.6	0	47.4	
2.6	50.0	1	44.4	3.0
2.9	47.1	2	41.2	3.2
3.3	43.8	3	37.5	3.7
3.8	40.0	4	33.3	4.2
4.3	35.7	5	28.6	4.7
4.9	30.8	6	23.1	5.5
5.8	25.0	7	16.7	6.4
6.8	18.2	8	9.1	7.6
8.2	10.0	9	0.0	9.1
10.0	0.0	10	—	—

spirometry in 38 normal subjects was for $QR \pm 5.4$ per cent. In a subject normally having 52.6 per cent of the perfusion through the right lung, the perfusion must go down to 47.2 per cent before it falls outside the tolerance interval. This figure corresponds to a loss of two "functional units" (Table 18). The tolerance interval for QRa was ± 7.9 per cent, corresponding to the loss of slightly more than one segment in an average subject (Fig. 25). In the right basal counting field, the loss of one "functional unit" corresponds to a decrease of 4.5 per cent. The tolerance interval for QRb was ± 5.4 per cent, thus somewhat more than one "functional unit" can be lost before an average subject will fall outside the range. The accuracy, thus estimated, was fairly equal for bronchspirometry and radiospirometry when judged from the function of each lung. If the radiospirometric data for the apical and basal fields, respectively, are studied separately, considerably smaller defects should be detected.

The percental distribution within both apical fields and both basal fields was preferred to the left/right ratio, as it permits a direct evaluation of the magnitude of the functional differences between the right and the left field. It also facilitates mathematical work with these parameters in pathological materials.

Right lung

Q R

Normal distribution: 10:19 = 52.6 %

Decrease after the loss of

1 unit	10:19 — 9:18 =	2.6 %
2 units	10:19 — 8:18 =	5.5 %
3 units	10:19 — 7:16 =	8.8 %
4 units	10:19 — 6:15 =	12.6 %

Number of
"functional units"



Q R a

Normal distribution: 4:8 = 50 %

Decrease after the loss of

1 unit	4:8 — 3:7 =	7.2 %
2 units	4:8 — 2:6 =	16.7 %
3 units	4:8 — 1:5 =	30.0 %

Q R b

Normal distribution: 6:11 = 54.5 %

Decrease after the loss of

1 unit	6:11 — 5:10 =	4.5 %
2 units	6:11 — 4:9 =	10.1 %
3 units	6:11 — 3:8 =	17.0 %

Left lung

Q L

Normal distribution: 9:19 = 47.4 %

Decrease after the loss of

1 unit	9:19 — 8:18 =	3.0 %
2 units	9:19 — 7:17 =	6.2 %
3 units	9:19 — 6:16 =	9.9 %
4 units	9:19 — 5:15 =	14.1 %

Q L a

Normal distribution: 4:8 = 50 %

Decrease after the loss of

1 unit	4:8 — 3:7 =	7.2 %
2 units	4:8 — 2:6 =	16.7 %
3 units	4:8 — 1:5 =	30.0 %

Q L b

Normal distribution: 5:11 = 45.5 %

Decrease after the loss of

1 unit	5:11 — 4:10 =	5.5 %
2 units	5:11 — 3:9 =	12.2 %
3 units	5:11 — 2:8 =	20.5 %

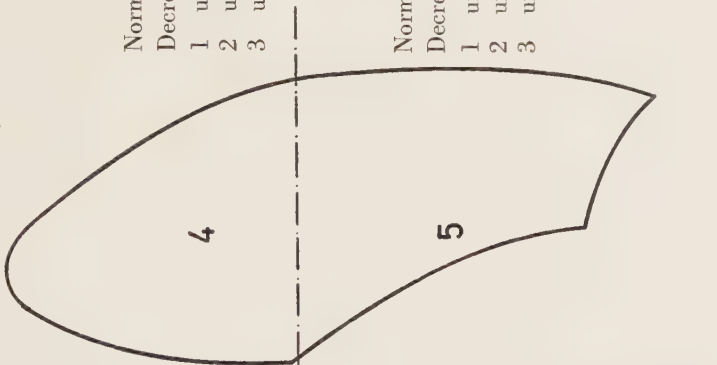


Fig. 25. Theoretical influence on the distribution of function from the loss of functioning lung tissue in different lung regions.

When developing the technique, it was decided to inject Xe-133 during apnea for estimation of relative perfusion. In order to reduce the need for cooperation from the patient it should be better to give the injection during the normal breathing (Heckscher et al. 1966).

The random error was found to be slightly greater than with estimations during breath-holding (Table 14, p. 66). The determinations during apnea and maintained breathing showed essentially good agreement, but when there was a pronounced unevenness in the distribution of perfusion and/or ventilation between the lungs, there was a tendency to overestimate the function of the diseased lung, when the examination was performed during maintained normal breathing (Tables 15 and 16, pp. 66—67). The differences were, however, rather small. The results of this comparison should justify injection during maintained breathing in clinical routine work.

Indications for regional lung function studies in clinical routine work

Indications for radiospirometry in the clinic cannot as yet be regarded as having been clearly established, but it seems reasonable that its indications can be essentially broader than those valid for bronchosprometry.

The most common indication for bronchosprometry is examination of the distribution of lung function before lung surgery. Regional lung function studies might be considered unnecessary in cases with good total lung function, as judged by spirometry. However, in cases having a moderate reduction of function (MVV 50—60 L/min.), it is possible that the greater part of the function will be in the lung that is to be operated on. Bronchial carcinoma is common among persons having chronic bronchitis and emphysema, both being diffuse lung diseases which lead to a general functional reduction that might be much more pronounced on the non-cancerous lung. Similar conditions can exist with tuberculosis of the lung, as in the following case:

Case 1. Male, 33 years of age, who had tuberculosis in both lungs 10 years prior to the investigation, and had been treated with bilateral artificial pneumothorax for 5 years. Patient was admitted to be operated for suspected cavern in the right lung as conservative treatment had not been successful.

X-ray showed bilateral pleural fibrosis, especially apically, but on the left side only slight parenchymal lesions.

Spirometry and bronchosprometry were performed before operation (Table 19).

This case showed that the function of the left lung was unexpectedly bad, which could not have been discovered without regional lung function studies. Surgery was, however, considered to be definitely indicated. In view of the results of bronchosprometry, it was planned to resect as little lung tissue as possible. Controlled res-

Table 19

Case 1. Male, 33 years of age.

Spirometry

VC	3.1 L	(59 % of predicted value)
FRC/TLC	71	(139 % „ „ „)
MVV	60 L/min.	(35 % „ „ „)
Lung clearance index	13.3	

Bronchspirometry

The function of the right lung in per cent of total function

Ventilation	69
O ₂ -uptake	67
FRC	68

piration was thought necessary during the post-operative period. Two segments were resected, one in the upper lobe, and one in the lower lobe. Post-operatively the patient was ventilated with a respirator for approximately 2 weeks.

It has been observed in this laboratory (Arborelius & Svanberg 1959) that in cases with centrally located bronchial carcinoma, the perfusion of the affected lung is usually more reduced than ventilation. Several authors have found remarkably large defects of perfusion in lungs with centrally located carcinomas, using lung scanning with non-gaseous tracers, and these have not corresponded to any changes in that area which appeared in the X-ray. (Wagner, Lopez-Majano & Tow 1965; Meldolesi, Martinenghi & Tarolo 1967; Ernst 1967). A low ind. Q and high V/Q ratio within a counting field affected by a centrally located tumour of unknown nature ought, thus, lead to the suspicion of primary lung carcinoma. This was true in the following case:

Case 2. Male, 70 years of age Diagnosis: Carcinoma bronchiale sin. cum metast. X-ray of the lung showed enlargement of the left hilus, but no parenchymal lesions were present. A lymph node, surgically removed from the supraclavicular fossa, showed tumorous growth having the appearance of bronchial carcinoma.

Spirometry showed nearly normal lung volumes and normal ventilation capacity, but the increased lung clearance index indicated uneven intrapulmonary gas distribution. The arterial oxygen tension was also slightly reduced (Table 20).

Radiospirometry showed a slight reduction of ventilation in the left apical counting field. No significant reduction of ventilation (V L) occurred in the left lung as a whole. Perfusion (Q L) was considerably reduced in the left lung. Index V was within normal limits for all counting fields. Index Q was pathologically reduced for the left apical field, as well as for the entire left

Table 20

Case 2. Male, 70 years of age.

Spirometry

VC	5.4 L	(117 % of predicted value)
FRC/TLC	61	(109 % " " ")
MVV	106 L/min.	(87 % " " ")

Lung clearance index 10.3

 P_{aO_2} 71 mm Hg P_{aCO_2} 36 mm Hg
Radiospirometry

Right				Left	
ind. Q II	1.11	Q L	29.4	ind. Q I	0.30
IV	1.38	V L	41.6	III	1.16
R	1.24	FRC L	43.2	L	0.68
		VC L	47.6		
ind. V II	0.98			ind. V I	0.82
IV	1.07			III	1.14
R	1.03			L	0.96
V/Q II	0.88			V/Q I	2.73
IV	0.78			III	0.98
R	0.83			L	1.41

lung. The V/Q was abnormally high for the left apical field and for the entire left lung. The V/Q for the right basal field and the entire right lung are not to be interpreted as indicating abnormal function in these areas (See example on p. 70).

If the total function is low (MVV <50 L/min.), it is even more probable that a regional lung function study can reveal facts which could be decisive for surgery. Considering the empirical experience that dyspnea at rest arises at a MVV of 20—30 L/min., it is possible to use spirometry combined with regional lung function studies to judge preoperatively if the lung tissue that will remain after the planned surgery will be sufficient to allow the patient to live without artificial respiration. For this purpose, radiospirometry yields information which is equivalent to that given by bronchspirometry, but also provides a more detailed picture of the distribution of function, as four counting fields are measured, instead of each lung separately, as in bronchspirometry.

It must be strongly emphasized that both bronchspirometry and radiospirometry, as used here, give only relative values for the function of each lung. The results of both methods must thus be evaluated against the background of the total lung function as estimated with conventional spirometry.

SUMMARY

The aim of this work was to develop a method using radioactive Xe-133 and external detectors which could replace bronchospirometry in clinical routine.

On the basis of the previous literature (Chapter I), theoretical considerations (Chapter II), and model experiments (Chapter III) the apparatus and procedure described in Chapter III were developed.

The new technique, here called radiospirometry, was tested against bronchospirometry in 35 patients with varying degrees of pulmonary disease (Chapter IV). The agreement between the two techniques was very good as regards the measurements of the distribution of perfusion, ventilation and vital capacity. The agreement was less good but still satisfactory in the estimate of the distribution of functional residual capacity.

In view of this excellent agreement between the two methods it was decided to study the variation of the radiospirometric measurements of regional lung function in normal men and women (Chapter V). The mean values for the right lung's part of the total perfusion, ventilation and vital capacity obtained with radiospirometry in normal subjects were almost identical with corresponding measurements obtained with bronchospirometry in normal subjects by Svanberg (1957).

The reproducibility of radiospirometry was better than that of bronchospirometry as regards measurements of the right lung's part of total pulmonary function (Chapter VI).

Measurements of regional perfusion made during apnea and during maintained normal breathing are presented in Chapter VII. Measurements during maintained breathing tended to overestimate the perfusion of poorly functioning parts, but the error was comparatively small.

Chapter VIII contains a discussion of the limitations and indications for radiospirometry as compared to bronchospirometry. It also illustrates the interpretation of the radiospirometric measurements and stresses the importance of conventional spirometry as a basis for the evaluation of the radiospirometric results.

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Mr. K. D. Muir revised the manuscript.

APPENDIX

Table 1

No.	Sex	Age	VC		TLC		FRC/TLC		FEV _{1.0}		Lung clear. index	Blood gases		Clin. diagnosis
			obs. value	% of pred.	obs. value	% of pred.	obs. value	% of pred.	obs. value	% of pred.		PaO ₂	PaCO ₂	
1	m	67	1.80	49	3.72	63	63	113	1.45	60	6.4	69	40	Carcinoma bronchiale sin.
2	m	58	2.90	71	4.89	79	59	107	2.25	78	8.5	74	38	Carcinoma bronchiale sin.
3	f	52	2.75	90	4.78	111	54	110	2.10	88	8.5	72	41	Neurofibroma mediastini.
4	f	58	2.40	78	4.02	89	46	96	1.90	82	7.8	73	37	Eventratio diaphragmatica sin.
5	m	76	2.30	59	4.31	68	71	125	1.63	69	10.4	73	35	Tumor malign. pleura sin.
6	m	65	2.35	59	4.64	72	68	117	1.48	56	7.8	81	38	Tuberculosis pulm.
7	f	62	2.40	87	4.42	109	57	114	1.65	80	7.1	87	34	Fibrosis pulm.
8	m	62	3.40	80	5.94	90	59	109	2.50	86	8.6	79	33	Carcinoma bronchiale sin.
9	f	56	2.40	79	3.79	86	51	104	1.85	79	9.2	70	38	Carcinoma bronchiale sin.
10	m	64	4.60	101	8.88	136	70	135	2.90	94	9.5	69	36	Bronchitis chron. c.
11	m	70	2.94	68	6.74	100	73	130	1.25	44	—	60	42	Bronchiectasiae emphysema pulm.
12	m	55	3.36	69	5.50	80	60	115	2.38	69	9.9	74	40	Carcinoma bronchiale sin.
13	m	46	3.91	82	7.03	108	56	110	3.15	88	6.9	71	38	Status post pleuritis sin.
14	m	70	5.44	117	8.06	112	61	109	3.05	101	10.3	71	36	Carcinoma bronchiale sin.
15	m	63	3.78	90	5.70	86	66	118	2.20	77	12.8	82	39	Carcinoma bronchiale c. metast.
16	m	53	3.16	66	5.37	79	64	123	1.85	54	10.4	67	39	Carcinoma bronchiale sin.
17	f	35	3.52	94	5.25	103	62	135	2.95	97	6.8	85	32	Bronchiectasiae pulm. sin.
18	m	59	4.32	95	7.12	103	65	118	2.85	90	9.3	71	40	Carcinoma bronchiale sin.
19	m	52	3.60	76	7.51	111	66	125	1.75	51	9.6	80	40	Susp. tumor pulm. sin.
20	f	61	2.53	91	4.57	113	61	122	1.90	91	11.3	67	41	Tuberculosis pulm.
21	f	37	3.45	102	5.80	128	63	134	2.85	102	6.9	78	39	Bronchiectasiae pulm. dxt.
22	m	66	3.29	85	5.84	94	63	111	1.65	65	11.0	63	45	Pneumoconiosis
23	f	48	2.42	91	4.71	132	75	153	1.75	80	12.5	71	37	Bronchitis chron.
24	m	66	3.44	79	6.81	102	64	116	1.30	45	9.7	70	38	Emphysema bullosa
25	m	56	4.20	94	7.06	103	70	127	2.00	63	10.3	75	34	Carcinoma bronchiale sin. Atelectasis lob. intermed.
26	m	74	2.84	83	5.33	94	68	117	2.10	102	11.5	83	35	pulm. dxt.
27	m	66	3.90	104	6.84	113	71	125	2.50	102	—	85	46	Carcinoma bronchiale dxt.
28	m	59	3.95	92	6.91	105	67	120	2.65	89	8.9	72	40	Tuberculosis pulm.
29	m	74	3.50	82	6.08	88	67	116	1.80	67	9.7	62	38	Carcinoma bronchiale dxt.
30	m	58	3.90	89	6.00	95	49	94	3.00	98	10.5	74	39	Carcinoma bronchiale dxt.
31	m	42	4.00	87	5.96	92	61	117	3.10	88	9.3	84	42	Tuberculosis pulm.
32	m	58	3.35	78	5.25	84	61	115	2.00	67	9.1	85	33	Carcinoma bronchiale dxt.
33	m	72	2.83	70	5.15	81	57	102	2.05	76	9.0	78	37	Carcinoma bronchiale dxt.
34	m	40	3.30	72	4.59	73	51	100	2.40	68	9.4	88	40	Tuberculosis pulm.
35	f	58	2.02	64	3.57	77	57	116	1.45	61	9.3	79	40	Bronchiectasiae pulm. dxt.

Table 2

Results of bronchspirometry (Br) and radiosprometry (Ra) in 35 patients with lung disease.
The figures indicate the perfusion, ventilation, FRC and VC of the right lung in per cent of the function of both lungs.

No.	Perfusion			Ventilation			FRC			VC		
	Br	Ra (QR)	Diff.	Br	Ra (VR)	Diff.	Br	Ra (FRCR)	Diff.	Br	Ra (VCR)	Diff.
1	100	77	-23	100	97	3	60	90	+3	100	100	0
2	100	91	-9	74	74	0	61	63	+11	63	68	+5
3	92	76	-16	85	90	+5		72		68	65	-3
4	75	68	-7	76	75	-1		64		68	52	-16
5	74	70	-4	70	77	+7		66		66	56	-10
6	70	68	-2	64	62	-2	65	57	-8	66	60	-6
7	70	62	-8	63	75	+12		59		56	56	
8	70	63	-7	57	61	+4	58	66	+8	58	57	-1
9	66	62	-4	59	50	-9	70	61	-9	58	53	-5
10	64	67	+3	64	61	-3	64	60	-4	54	58	+4
11	63	61	-2	71	73	+2		55		60	60	
12	62	69	+7	75	75	+10	55	65	+10	62	68	+6
13	61	71	+10	63	73	+2		63		62	63	+1
14	60	57	-3	56	58	+2	55	57	+2	55	52	-3
15	59	61	+2	60	58	+8	62	58	-4	61	60	-1
16	59	55	-4	52	71	+11		54		49	56	+7
17	59	60	+1	50	58	+6	52	55	+3	58	57	-1
18	59	59	+1	50	62	+12	65	62	-3	53	56	+3
19	58	59	-1	50	59	+9	51	54	-2	61	49	-4
20	57	56	-1	59	57	-2	56	56	+9	51	49	-2
21	52	49	-3	53	51	-2	42	51	+4	52	52	
22	52	55	+3	52	60	+8	49	53		51	51	
23	52	56	+4	49	57	+8		53	+7	53	50	-3
24	51	51	+6	53	55	+12	46	53		53	53	
25	51	57	+8	47	59	+4		57		45	48	+3
26	48	40	-8	51	40	-11		46		52	50	-2
27	48	52	+4	50	46	+4	45	52	+7	54	50	-4
28	48	50	+2	48	52	+4	46	45	-1	47	45	-2
29	42	39	-3	33	33	0		45		44	41	-3
30	41	48	+7	45	49	+4	36	48	+5	44	41	-3
31	39	42	+3	45	44	-1	43	41	+6	48	48	0
32	36	35	-1	20	38	+18	45	49	-2	42	43	+1
33	34	37	+3	42	37	-5	33	43	+1	29	32	+3
34	30	27	-3	35	23	-12		34		34	34	0
35	18	24	+6	39	32	-7		38				

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